PREFACE

THIS Report provides the first complete account of an investigation, by the Council's Clinical Research Unit under Dr R T Grant, into the systemic results of violent injury The work was undertaken at the request of the Committee on Traumatic Shock, and was begun at Guy's Hospital and at neighbouring hospitals during the air raids of 1940 and 1941 When large-cale raids on London ceased, it was continued at the Royal Victoria Infirmary, ewcastle-on-Tyne, on patients injured in industrial and road accidents The al stage was carried out between 1944 and 1945 on the Italian battlefront various times the authors were assisted by Drs N A Neville, H H wiatkowski, E D Barlow and F R Robertson, and by Majors R P arbord and R J Rossiter, R A M C

The authors' particular contribution is in the sphere of clinical definition ney believed with other workers that much discussion on the subject of 'ound shock' was vitiated by the fact that different writers were in fact dis-issing a variety of different conditions They therefore set out to obtain full scriptions of the clinical state of patients who had suffered severe injuries the course of five years they saw over three hundred such patients, follow-ng them continuously either until death or until recovery seemed certain The detailed histories of these patients provide a mass of information that is likely to be of great value to later workers

The authors found that the various signs following injury occurred in a number of distinct patterns, and they were able to relate most of these patterns to particular sets of causative factors They paid most attention to haemorrhage, as the major contributing factor, and thus to transfusion as the nost valuable form of treatment By correlating their clinical observations ith carefully controlled blood volume measurements they succeeded in evolving simple and reliable clinical methods for assessing the amount of blood lost and the amount of transfusion required Attention was also paid to e disturbances of water and electrolyte balance that may follow abdominal iuries, and to the dangers of bad anaesthesia and rough handling

The injuries suffered by these patients were almost all due to war But they ave many counterparts in the accidental injuries of civil life, and it is hoped hat the observations recorded here will therefore be as useful to the civilian is to the military surgeon

MEDICAL RESEARCH COUNCIL, *October* 11, 1951
38 Old Queen Street,
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NOTE

Since some of the case histories in this book are very long, the most important part of each has been marked off by stars (*) inserted in the text

OBSERVATIONS ON THE GENERAL EFFECTS OF INJURY IN MAN

WITH SPECIAL REFERENCE TO WOUND SHOCK

BY

R T GRANT, O B E, F R C P, F R S and E B REEVE, B M., M R C P

from the Clinical Research Unit of the Medical Research Council, Guy's Hospital

GENERAL INTRODUCTION

THE five years' work described in this Report was begun during the London air raids in 1940 Its initial object was to learn to recognize and treat the condition known as traumatic or wound shock, which was reported to be occurring frequently in air raid casualties We soon found ourselves discontented with the conception of shock as it had been variously defined in past writing on the subject

From time to time others have protested that the word "shock" was unsatisfactory and that confusion arose from its continued use Most of the complaints have been of the lack of a generally acceptable definition of the word, but continued attempts at definition have increased rather than diminished the confusion (see for example Harkins's review of traumatic shock (Harkins, 1941))

Several factors contribute to this confusion Firstly, the word "shock" is commonly used in two different senses to mean, on the one hand, a pathological state or process and, on the other, a clinical syndrome, often without any clear indication of which sense is intended Sometimes it is used first in the one sense and then a little later in the other, apparently without the user being aware of the change Such a usage must inevitably cause confusion and contradiction For example, the answer to the question whether or not "haemoconcentration" is a sign of "shock" depends on how the word "shock" is used If it is intended to mean a pathological state of reduced blood volume due to plasma loss, then an abnormally high proportion of red cells in the blood is an essential part of the condition and it is unjustifiable to call a patient "shocked" unless it can be demonstrated On the other hand, if the word is used to mean the syndrome of low blood pressure, skin pallor and coldness, and rapid pulse, then the presence or absence of haemoconcentration is irrelevant to diagnosis, which can be made in the presence of all the above signs and on no other grounds In similar ways confusion has arisen about almost every sign and symptom that can be elicited from the "shocked" patient

As a result, many statements are made that to one man seem true and to another false, for example, that the first thing the clinician should learn is that there is hardly one sign of shock which is constant This statement is sense or nonsense according to the view taken of "shock" If "shock" means a state of reduced blood volume then its clinical expression may well vary with a number of factors, for example with the rate and degree of reduction, so that blood pressure may be high, low or normal, and pulse rate slow, fast or

normal, but if it means the syndrome of low blood pressure, fast pulse, skin pallor and coldness, then by definition the signs are constant

It seems needless to multiply examples, it is an instructive exercise for readers of the writings on "shock" to attempt to define the sense each time the word is used, when the confusion is readily made manifest

The manner of using the word affects the problem facing the clinician For example, for one man the problem is to recognize a state of reduced blood volume in all its manifestations, while for another it is to interpret a defined clinical picture in terms of its causative factors, of which reduced blood volume may or may not be one

Our first task was diagnosis, so that we were primarily concerned with "shock" as a clinical syndrome Like many other workers at the beginning of the war, we had little or no experience of wounded men and had to rely mainly on descriptions given by others Recognition of an unfamiliar picture from description is the more certain the more closely the picture corresponds in all its details with the description But here we came up against a second difficulty For we found that, while the various descriptions of shock in the literature bore a general resemblance to each other, they differed in detail Moreover there seemed to be no agreement as to which of the features most commonly mentioned were essential for diagnosis and which were secondary in importance Some authorities said "no low blood pressure, no shock", others that blood pressure is an unreliable index of shock, that severe shock might exist with normal blood pressure and that "haemoconcentration is the earliest detectable manifestation of shock as well as the most accurate index of its severity" (Moon, 1938)

In practice we found that the diagnosis of shock seemed to depend on the personal views of the individual making it rather than on generally accepted criteria Unless we were acquainted with these views we did not know what to expect when called to the bedside The label alone did not indicate what signs and symptoms the patient displayed, how ill he was or what treatment he required The only common ground for diagnosis that we could detect was that the patient seemed *ill*, the criteria of illness were obscure, though facial pallor seemed to be a feature much relied on

It seemed important, because of the differing treatments required, not only to recognize wound shock but to distinguish between primary and secondary wound shock and to differentiate them from shock due to haemorrhage All three were said to be closely similar in their clinical manifestations Again the criteria used for differentiation, at least between primary and secondary wound shock, differed from author to author, the only general distinctions were that primary shock was said to develop immediately or soon after injury, secondary shock to come on insidiously some hours after injury Secondary wound shock was distinguished from that due to haemorrhage by the fact that it resulted in concentration, and haemorrhage in dilution, of the blood

A further cause of confusion and uncertainty was the serious lack of adequate description of cases said to be "shocked" We could not find in the literature any sufficient account of injured patients such as those we saw daily in the wards, of whom we have already published illustrative case histories

(Grant and Reeve, 1941) We often saw patients with pale faces and cold extremities, but their pulse rates ranged from slow to fast and their blood pressures from high to low, none displayed haemoconcentration, and weakness, apathy, shallow and rapid breathing were not characteristic We were therefore in much doubt whether or not they were "shocked", if they were, we were uncertain if the "shock" was primary or secondary, or due to haemorrhage

In short, we could not obtain, either from our reading or from our more experienced colleagues, clear and generally acceptable indications by which to recognize secondary wound shock, to differentiate it from the other types of "shock", or to decide such practical points as which patients should be transfused, whether blood or plasma should be given, when to transfuse, how much to transfuse, and when to operate These matters were in practice decided by "clinical judgment", and the decision varied with the clinician

We were led, therefore, to discard the word "shock" in its varying definitions We have not since found it of any value in the study of injury, it has rather been a hindrance to unbiased observation and a cause of misunderstanding For further discussion of this confusion, see Part III, p 182

It was soon clear that *a first requisite towards resolving confusion and* bringing order into the diagnosis and treatment of the general effects of injury was to become intimately acquainted with the details of the patients' state and course Only in this way did it seem possible to learn whether injury produces *only one, or several different or allied states of illness*, what are the factors producing these states and how to treat injured patients

The study proceeded in three stages In the first stage the patients observed were mostly air raid casualties, but included as well a number of accidental injuries and surgical emergencies, the only types of injury excluded were burns and those resulting from prolonged compression (the so-called "crush syndrome") The results (Grant and Reeve, 1941) suggested that (1) though the phenomena presented by injured patients varied, they could be grouped into several more or less well-defined syndromes, and (2) blood loss is the most important, but not the only, factor producing illness after injury

In the second stage of the investigation special attention was paid to limb injuries, since injuries to different parts of the body differ significantly in course and treatment, and require separate study, while limb injuries are the most common and involve no vital structures, and it is easier to assess the extent of blood loss and tissue damage in them than in any other form of injury The report on this second series of patients (1) further defined the syndromes described in the first report, (2) offered evidence that they are brought about by varying combinations of three main factors blood loss, tissue damage and nervous disturbance, and (3) gave greater precision to the rules for diagnosis and treatment.

But it also pointed to a need for still more study of two factors in particular, tissue damage and blood loss This third stage in the investigation was carried out on battle casualties in Italy, among whom were many cases of large limb injuries It provided *evidence that, at least in the early stages, the only major factor producing serious illness is blood loss* The high death rate (over 60 per cent) of patients with very large limb injuries, which we had previously

ascribed to the absorption of toxic substances from damaged tissue, we now realized to be due to failure to recognize the grossness of the haemorrhage and to give sufficient blood by vein sufficiently early and quickly

We also studied cases of abdominal injury Since before going to Italy we had had little experience of this group, a great part of our work with them was to become acquainted with the details of their state and course, to determine the part played by blood loss and to disentangle the effects of treatment before, during and after operation Although abdominal injuries differ from limb injuries in a number of respects, they resemble them in that haemorrhage is an important factor influencing initial state, before the development of peritonitis it may be said to be the chief factor, and certainly much depends on its proper treatment

In this report the results of all these investigations are now gathered together Parts I and II deal particularly with the clinical aspects of the work, on patients suffering from injuries to the limbs and abdomen respectively In Part III our findings are brought into relation with those of other workers, and Part IV discusses the more technical aspects of the work on blood volume measurements, on the haematological changes and on certain biochemical features associated with injury

PART I

INJURIES TO THE LIMBS

The Patients, their Injuries and Blood Loss

PATIENTS

OUR evidence is derived from the study of two series comprising in all 230 patients The first series, of 120 patients, was observed in England from the autumn of 1940 until the end of 1943 The second, of 110 patients, was observed at forward Casualty Clearing Stations or Field Dressing Stations during the campaign in Italy, from April 1944 till the end of hostilities in May 1945 These two series have enabled us to see the results of injuries to limbs caused in different ways in patients of both sexes and all ages and under a wide variety of circumstances

Neither series is a representative sample of the patients with limb injuries admitted to hospitals at home or in the field For both include an unusually high proportion of the more seriously injured and of those regarded by our colleagues as being "shocked", while the less severely injured were observed either because they displayed unusual features of interest, such as pallor or high or low blood pressure, or in order to obtain a sufficient number of cases for comparison with those suffering from the larger injuries

The general method of study throughout has been to follow a patient closely at the bedside from the time of admission to hospital or soon after, through operation, and afterwards until recovery seemed assured or until death supervened, and in the latter case to examine the body after death This programme was achieved for almost all the patients, but a few did not come under observation till after operation

The 110 patients seen in Italy were nearly all fit soldiers, mostly our own troops, though 8 were prisoners of war and 13 were Italian peasants, 2 of them women With the exception of 5 men in the fighting services, the Home patients were civilians, of whom 23 were women

The ages of the patients are shown in Table 1 In the Italian Series, ages ranged from 10 to 60 years, with an average of 28 years The great

TABLE 1

Ages of patients with limb injuries

Series	Age (years)							Total
	10–19	20–29	30–39	40–49	50–59	60–69	70–79	
Italian	3	71	27	7	1	1	—	110
Home	17	26	24	16	19	12	6	120

majority (89 per cent) were in the twenties and thirties The Home Series included a considerable proportion of older persons, ranging in all from

10 to 71 with an average of 38 years Only 41 per cent were in their twenties and thirties, while 45 per cent were aged 40 or over

INJURIES

In just under half of the Home Series the injuries were due to air raids and in the remainder to industrial and road accidents Accident accounted for only nine of the Italian Series, the injuries in the others being caused by mines, booby traps, high explosive shells, mortar bombs, bullets and other weapons of war The injuries ranged from minor cuts, bruises and abrasions to gross destruction of one or more limbs They mainly affected the limbs but were not confined to them, a few were injuries to the soft parts elsewhere, the head, neck, and trunk, but they did not involve the contents of the skull, thorax or abdomen They are classified on an estimate of the volume of tissue damaged, as judged by inspection of the wounds on admission, at operation and after death As a guide to the volume of damaged tissue the patient's hand is taken as the unit The open hand may be used to assess the damage in superficial wounds, and the closed hand to estimate the volume of a bruised or pulped segment In a man of average size the volume of the hand, open or closed, is just under ½ litre The foot, knee, forearm and upper arm are approximately equal in volume (the foot and knee each rather less, and the upper arm rather more than the forearm) and each is roughly equal to 2–3 times the volume of the hand Leg volume is 4–5 times and thigh volume 10–12 times that of the hand

The injuries are grouped under four categories according to size in terms of the volume of tissue judged damaged (1) small wounds, with damage of less than 1 hand, (2) moderate wounds, with damage of 1 hand or more but less than 3 hands, (3) large wounds, with damage of 3 or more, but less than 5 hands, (4) very large wounds, with damage of 5 hands or more in volume *

The following examples illustrate the types of wounds in the different categories

(1) *Small wounds* damage less than 1 hand
   (a) Works accident, compound dislocation of the elbow, 2 in humerus protruding in front through a tear in the skin, no fracture or muscle damage, brachial artery severed
   (b) Air raid casualty, bruised arm small incised wounds of wrist, scalp, face and chest wall
   (c) Battle casualty, perforating bullet wound of the forearm

(2) *Moderate wounds* damage of 1 hand or more but less than 3 hands
   (a) Pit accident, compound fracture of the femur at the junction of the upper and middle thirds, with a clean 3 in cut above it, femoral artery intact little bruising of the muscles
   (b) Air raid casualty, leg torn off through the lower thigh, 2–3 hands of damaged tissue in the stump
   (c) Battle casualty, wound 2–3 in square on the calf, mainly involving skin and subcutaneous tissue, two penetrating wounds in the calf with about a fist of torn discoloured and infected calf muscle

* The same terms were used in our second report with different meanings Small wounds there implied damage of less than ¼ hand moderate wounds ¼–1 hand large wounds, 1–2 hands, very large wounds, more than 2 hands The revision of the grouping is due to the greater number of cases with very large wounds in the Italian as compared with the Home Series

(3) *Large wounds* damage of 3 or more hands but less than 5
   (a) Car accident, compound fracture of right femur, compound fracture of right tibia and fibula, considerable laceration of the muscles
   (b) Air raid casualty, left leg blown off through the knee, compound fracture of right tibia and fibula, with muscles badly lacerated
   (c) Battle casualty, compound fracture of the lower third of the right tibia, six penetrating wounds in the right calf, with much swelling and damaged muscle

(4) *Very large wounds* damage of 5 or more hands
   (a) Railway accident, compound fracture of the lower end of the right femur with a large wound, at least the lower half of the thigh badly crushed, bruised and swollen, a compound fracture of the right tibia and fibula at the junction of the lower and middle third, stump crushed, right foot crushed and hanging by the skin only, 3 in cut on the dorsum of the left foot and some crushing of the tissues
   (b) Air raid casualty, compound fracture of the left femur, extensive muscle laceration in the thigh, compound fracture of the right radius and ulna and much laceration of the soft tissues
   (c) Battle casualty, partial traumatic amputation of both feet, both legs mangled to the knees, small wounds of the right arm

TABLE 2

Cases grouped according to volume of tissue damaged

	Small wounds (<1 hand)	Moderate wounds (1 to <3 hands)	Large wounds (3 to <5 hands)	Very large wounds (5 hands or more)
Italian Series (110 cases)	27 (Cases 1–27)	44 (Cases 28–71)	21 (Cases 72–92)	18 (Cases 93–110)
Home Series (120 cases)	45 (Cases 1–45)	55 (Ca es 46–100)	10 (Cases 101–110)	10 (Cases 111–120)
Total (230 cases)	72	99	31	28

Table 2 shows the injuries of both series classified in this way The cases in each series are numbered approximately in order of increasing wound size In the following text, cases of the Home Series are denoted by the letter H, and those of the Italian by the letter I, preceding the serial number

Comments To avoid errors in classification, we emphasize the need for careful examination of the wounds Long deep incised wounds and large superficial wounds give, by gaping, a first impression of extensive tissue damage, whereas close inspection shows that the tissues bordering the wound are apparently viable and at operation the surgeon has to remove less than ½ hand of damaged tissue On the other hand, dissection of a limb stump may reveal damage considerably greater than was suspected before

In making the estimate of tissue damage, the volume of any limb severed, or almost severed, from the body by injury is neglected, and only the injury to the limb stump is considered As evidence of such injury we take such

obvious signs as abrasion, bruising, tearing and discoloration of the soft parts, loss of contractility of muscles and fractures of bones In a number of cases the damaged tissue removed from the wound was weighed and the portions amputated from the limbs by the surgeon at operation were dissected

Though a proper estimation of this damage can often only be made at operation or necropsy, usually a sufficiently good estimate can be made when the patient is first seen, if the wounds are carefully examined

Classification in terms of volume avoids the implications associated with the terms slight or severe, more important, it allows cases where different parts of the limbs and soft tissues have been damaged to be classified according to the degree of tissue damage

BLOOD LOSS AND BLOOD VOLUME

Blood loss was assessed by two methods, (1) by estimations of the amount of blood shed into the wounds and on to the dressings and clothes, and (2) by measuring blood volume by the dye method

In the Home Series blood volume measurements were not made The amount of blood lost externally and into the tissues was estimated roughly by examination of the wounds, dressings and clothes The large majority of these patients were admitted within a short time of injury, dressed in the clothes they wore when injured and with the first aid dressings still applied to the wounds Sometimes we soaked the dressings in ammoniated water and estimated their blood content from the haemoglobin content of the watery extract Information was obtained when possible from the patient himself and from the attendants and the eye-witnesses of the accident who frequently accompanied him In this way it was possible to make reasonable estimates of blood loss, on the basis of which we have divided the cases into three groups (1) those losing less than 5 per cent of their blood volume, (2) those losing 5–20 per cent, and (3) those losing over 20 per cent In a man of average size, 10 per cent of the blood volume is about 1 pint or ½ litre

In contrast to the Home Series, the majority of the Italian cases offered little visible evidence on which to estimate their blood loss, for only a few cases injured by accident, mines or air raids in the neighbourhood were admitted directly to the Casualty Clearing Station at which we were working The majority had previously passed through a Regimental Aid Post and one or more Field Ambulance Posts, and by the time we saw them their torn and blood-stained clothing had been removed and their blood-soaked bandages replaced Only rarely had the medical officers who saw the patients earlier recorded evidence of bleeding and its degree In this series, therefore, haemorrhage was estimated from blood volume measured by the dye T1824

Blood volume was measured in 71 cases (twice in 37, and three times in 3 of them) In 43 it was measured soon after admission and in the remainder at varying times after operation Because of the difficulty of injecting dye into constricted vessels and withdrawing blood samples from them, and because of the danger of delaying transfusion, it was not possible to measure blood volume initially in more than a few of those who were seriously ill and whose blood volumes seemed to be likely to be greatly depleted In a number

of such cases and in a few others initial blood volume, though not measured, can be estimated by "back-calculation" from a later blood volume measurement Provided that the blood volume estimate was made within a few hours of admission and that it was known how much blood and plasma had been transfused and how much blood lost by haemorrhage between admission and the blood volume estimate, fairly reliable estimates of initial blood volume could be made The initial blood volumes, both measured and calculated, are shown in Table 6 (p 16), they are expressed as percentages of the predicted normal for height, using data from Gibson and Evans (1937) and assuming that the normal haematocrit is 47 per cent (see Part IV)

The amount of blood lost through haemorrhage by the time the patient came under observation can be calculated from the initially measured blood volume in 40 cases and "back-calculated" in 13 others Blood losses through haemorrhage have been expressed in terms of whole blood (haemoglobin 100 per cent normal) as a percentage of the total predicted normal blood volume (see p 233), and are shown in Tables 4, 5, and 6 (pp 12, 13 and 16)

It is necessary to distinguish between the amount of blood lost through haemorrhage and the actual reduction of blood volume Immediately after a man has lost blood by a rapid haemorrhage his blood volume is equivalent to his initial blood volume less the amount of blood lost But after this fluid is added to his blood and the volume increased If he bleeds further, he bleeds more dilute blood than his original blood, and his blood will be further diluted by the addition of more fluid Thus within a few hours after injury it is possible for a man who has bled and diluted his remaining blood to have a blood volume 70 per cent of its original value after having lost 40 per cent of his original blood In the cases observed at home, where the interval between injury and coming under observation was short, the difference between the blood loss and the reduction of blood volume is likely to have been small, so that here the estimate of blood loss is taken as an estimate of the reduction of blood volume

It is to be remarked that in none of the cases at home or abroad did initial examination of the blood reveal evidence of blood loss other than by haemorrhage None showed haemoconcentration, most showed dilution

Comment The estimates of blood loss in the Home Series may not be reliable and in some cases there was considerable doubt as to how much blood had been lost Nevertheless, we consider that they are of the right order for each wound size group taken as a whole

In the Italian Series, where direct evidence of blood loss was usually lacking, the patients' unsupported statements were not as a rule helpful, for many had no idea how much blood they had lost But on the whole those who gave an estimate of blood loss in terms such as "little", "a moderate amount" or "buckets of blood" were proved by blood volume measurements to have been approximately correct more often than not It is to be emphasized, however, that in these patients the absence of much blood on the clothes or dressings could not be taken as indicating that there had not been much previous blood loss Failure to realize this often resulted in trouble during the subsequent course of the patient

For convenience in the following account the measured blood volumes are stated to the nearest 1 per cent as percentages of the predicted normal blood volumes * This method of presenting values must not be taken to indicate that the estimates are of this degree of accuracy The methods used to obtain them are described later, and it is probable that their accuracy is, under favourable conditions and with good technique, of the order of $\pm$ 5 per cent We have preferred not to round off the values to the nearest 5 or 10 per cent, but to give them as calculated Similarly for a number of cases estimates of haemorrhage are quoted to the nearest 5 per cent Again no such accuracy is claimed for the results, which only indicate the order of haemorrhage We describe fully in Part IV (p 228) the methods used and the problems involved in the estimation of blood volume and haemorrhage in these patients We think that few of the estimates are grossly in error and that the values given can reasonably be used for the present analysis of the cases

Initial State

INTRODUCTION

In both series the injured patients were admitted to hospital (from ambulances) on stretchers, clothed and covered with blankets They were taken to the admission room and examined by the admitting officer Those thought to require it were sent to the resuscitation room wherever the hospital provided it, others were sent to await operation either in a surgical ward (the usual practice in civilian hospitals) or in the pre-operation room (in Casualty Clearing Stations) They were first seen by us on admission or soon after

In the Home Series the large majority came under observation within 2 hr of injury and almost half within 1 hr (Table 3) The shortest time was

TABLE 3

Interval between wounding and observation patients with limb injuries

Time (hr)	0–1	1 01–2	2 01–3	3 01–4	4 01–6	6 01–12	12 01–18	18 01–24	Over 24	Total
Italian† Series	4	7	5	15	20	31	9	8	1	100
Home Series	53	30	16	2	12	7	—	—	—	120

†Ten cases of the main series are omitted, since they were not observed till after operation

5 min and the longest 11 hr Most had received first aid treatment for their wounds, some had had tourniquets applied, only a few had been given morphine and none had been transfused Most were seen in the colder months, a few, in whom observation was delayed until some time after admission, had been warmed by hot water bottles or electric cradles

* At operation a number of patients lost by amputation sufficient tissue to reduce their blood volume significantly All subsequent blood volume estimations are therefore stated as percentages of a *reduced* predicted normal in which allowance has been made for loss of vasculature

In the Italian cases a longer time elapsed between injury and observation, in the case of a large majority between 3 and 12 hr (Table 3) The shortest time was ½ hr and the longest 52 hr (the only one over 24 hr) Only a few injured in the neighbourhood were admitted direct, with little or no treatment, to the hospitals at which we worked Most had been transported from the area of fighting by stretcher and ambulance for distances of 3–25 miles over rough tracks and roads, passing through Regimental Aid Posts and one or more Field Ambulance Posts They had been examined several times and given morphine ¼–½ gr, their wounds had been dressed at least once and their limbs splinted They had been given fluids to drink and almost a quarter had already received transfusion Most were seen in warm, some in hot and a few in very cold weather, those who had been exposed to cold had been warmed at some stage of their journey The rooms or tents in which we examined the cases were, in cold weather, warmed more or less efficiently by paraffin stoves

Comment A proper appreciation of their state when they are first seen is of prime importance in dealing with these patients, because the diagnosis made and the treatment prescribed as a result of the initial examination influence their further course greatly and may determine whether they live or die The initial states, like the wounds, varied greatly At the one extreme, some patients seemed relatively well, at the other, some seemed so ill as to be about to die

Case I 24, a soldier aged 29, was seen 6 hr after injury (small wounds laceration of calf), lying on a stretcher His face was well-coloured and his extremities were warm and not sweating, his blood pressure was 115/70, his pulse rate 88 He was mentally clear but apprehensive about his state He was not thirsty

Case I 82, a soldier aged 30, was seen 3 hr after injury (large wound shoulder destroyed) He was lying on a stretcher in the head-down position, very pale, quiet, with cold and sweating hands, and with an impalpable radial pulse and a carotid pulse palpable but poor in volume at a rate of 120 His blood pressure was 50/25 He was mentally clear, anxious and very thirsty

The problem was to know what observations would be of value We wanted to judge as early as possible how ill the patient was, what would happen to him and what treatment he required

It soon became clear that the predominant illness was a depression of the circulation Therefore special attention was paid to the state of the circulation and to four features in particular blood pressure, pulse rate, skin temperature of the extremities (mainly fingers, but also nose and ears) and colour of the face * Other features observed are referred to later

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* Skin colour and temperature provide evidence of the calibre of the cutaneous vessels and of the blood flow through them We have roughly assessed skin temperature, using the fingers as the usual site, by feeling the skin, after it had been exposed to room air for some time with our own warm hands

Only in the extremities is skin temperature a reliable index of skin blood flow The skin temperature of the forehead trunk and muscular parts of the limbs is largely influenced by the blood flow through underlying structures and may be warm although local blood flow through the skin is greatly reduced or at a standstill The observer s hand must be warm otherwise he will wrongly estimate the temperature of the palpated skin The extremity must have been exposed to the air for some time, a hand withdrawn from under the blankets or a heated cradle may be warm even if the blood flow is poor

Pallor of the face, though it may be due in part to reduction of the haemoglobin content of the blood and to lowering of blood pressure, is mainly due to an active constriction of the minute vessels, if these are dilated the face may be well coloured even though both blood pressure and haemoglobin are low (e g 60 mm Hg and 50 per cent)

Experience gradually accumulated to show that the initial circulatory state resulted from the interaction of a number of factors, one or other of which might predominate So far as they were recognized, these factors were, first and foremost, haemorrhage, and, of secondary importance, emotional and nervous stimuli, exposure to heat and cold, treatment before coming under observation and age It follows that in the initial state the physical signs demanding closest attention are those indicating blood loss Those of the greatest value are, first and most important, wound size and, secondly, the level of systolic blood pressure

WOUND SIZE RELATED TO BLOOD LOSS

Tables 4 and 5 show that in both series of cases there is a correlation between the size of the wounds and blood loss, in the sense that the larger the wounds the greater the blood loss

In the Home Series (Table 4) the great majority of those with small wounds are judged to have lost less than 20 per cent of their blood, and half of these

TABLE 4

Wound size related to blood loss patients with limb injuries, Home Series

Blood loss (per cent normal blood volume)	Size of wounds				
	Small (<1 hand)	Moderate (1 to <3 hands)	Large (3 to <5 hands)	Very large (5 hands or more)	Total
Under 5	18	—	—	—	18
5–20	19	20	—	1	40
Over 20	8	35	10	9	62
Total	45	55	10	10	120

less than 5 per cent, a negligible quantity On the other hand, all except one of those with large and very large wounds lost more than 20 per cent of their blood and none a negligible quantity Of those with moderate wounds the majority lost over 20 per cent

The correlation is better displayed by the 56 cases of the Italian Series in whom initial blood loss was estimated from blood volume measurements (Table 5 and Fig 1) Of the 14 patients with small wounds, 10 lost 20 per cent of their blood or less and 8 of these a negligible quantity The average blood loss of those with moderate wounds was about 30 per cent, though there was a wide scatter above and below this figure, from less than 5 to about 50 per cent. For large wounds the average blood loss was about 40 per cent and no patient lost less than 25 per cent Of the 10 patients with very large wounds 7 had lost more than 50 per cent of their blood and only 1 less than 40 per cent.

TABLE 5

Wound size related to blood loss 56 Italian patients with limb injuries

Small wounds (<1 hand tissue damage)			Moderate wounds (1 to <3 hands tissue damage)			Large wounds (3 to <5 hands tissue damage)			Very large wounds (5 hands tissue damage and more)		
Patient	Time seen after injury (hr)	Blood loss (per cent normal blood volume)	Patient	Time seen after injury (hr)	Blood loss (per cent normal blood volume)	Patient	Time seen after injury (hr)	Blood loss (per cent normal blood volume)	Patient	Time seen after injury (hr)	Blood loss (per cent normal blood volume)
I 1	4	<5	*I* 33	1¾	C40	*I* 73	5½	C45 ?	*I* 93	7¼	60
I 2	18	<5	*I* 35	19½	15	*I* 74	3¾	25	*I* 95	4	40
I 3	6½	5	*I* 37	2	<5	*I* 76	5¼	40	*I* 96	2	C55
I 6	1½	<5	*I* 39	17½	45	*I* 77	6¾	35	*I* 98	8	60
I 7	18½	<5	*I* 40	22½	25	*I* 78	3½	50	*I* 99	5¾	45
I 9	17	<5	*I* 41	5	5	*I* 79	8	40–45	*I* 101	2¼	C60 ?
I 12	22	<5	*I* 43	4¾	45	*I* 81	6	C45	*I* 104	3½	25–30
I 14	9½	<5	*I* 44	4	35	*I* 83	7	55	*I* 106	7¾	C60 ?
I 15	9	C 60 ?	*I* 45	5½	55	*I* 85	5	C55	*I* 109	10½	C60 ?
I 18	15	20	*I* 46	5½	40	*I* 86	6¼	35	*I* 110	1½	C60 ?
I 20	10	20	*I* 49	53	35	*I* 88	1	30			
I 23	19	50	*I* 51	5½	C25	*I* 89	14	C40 ?			
I 24	8½	25	*I* 53	6½	C50–60						
I 25	10½	45	*I* 55	4	40						
			I 57	1½	40						
			I 60	8	25						
			I 64	5	C25						
			I 66	6½	15						
			I 68	5	C35						
			I 70	8¼	C40						

C Values obtained by back calculation
? Values thought less reliable

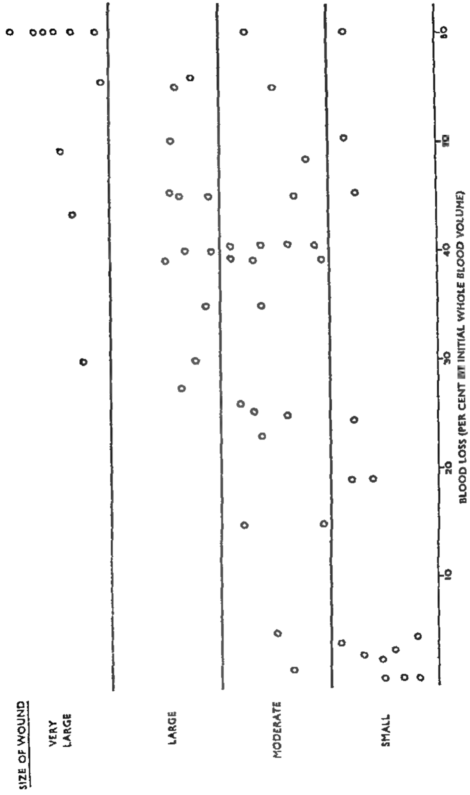

Fig 1 Estimated haemorrhage related to size of wounds

For comparable injuries there is no clear relation between blood loss and the time after injury at which it is estimated, it is probable that the greater part of the blood is lost soon after injury

In the Home Series the clinical estimates of blood loss were purposely conservative, any considerable blood loss being noted as "over 20 per cent" Had blood volume estimates been made it is almost certain that they would have given greater values Supporting evidence for this statement will be found in the work of others discussed later (p 198) Hence the blood loss shown as over 20 per cent for the Home Series in Table 4 must be interpreted as materially greater in large than in moderate wounds, and in very large than in large wounds

Thus in general those suffering small wounds lose little blood, rarely more than 20 per cent of their initial blood volume and commonly less than 10 per cent Note that it is because we were particularly looking out for cases with small wounds and considerable blood loss that an appreciable proportion of those with small wounds in Tables 4 and 5 show blood loss greater than 20 per cent Such cases were rare With large wounds, on the other hand, much blood is lost, of the order of 40 per cent, and with very large wounds very much, of the order of 50 per cent Moderate wounds give a less clear indication of blood loss, it may be much or little, though in the majority it is of the order of 20–40 per cent

BLOOD PRESSURE RELATED TO BLOOD LOSS

In Table 6 blood loss, blood volume and blood pressure are shown for 51 individual patients of the Italian Series We consider now only the 39 cases not previously transfused, those transfused before being seen are dealt with later (p 23)

Blood pressure is in general related to blood loss, those losing not more than 30–40 per cent of their original blood had blood pressures of 100 mm Hg or more But it is more closely related to blood volume Table 6 and the summary of its data given in Table 7 show that (i) with only one exception, those with blood volumes of 70 per cent normal or more have blood pressures of 100 or more, and (ii) again with only one exception, those with blood volumes of less than 70 per cent normal have blood pressures of less than 100 In the two exceptions, blood volume is not much above or below 70 per cent (74 and 67 per cent)

The number of untransfused cases with blood volumes measured or calculated to be under 70 per cent is small, owing to the technical difficulties already alluded to (p 8) To this number we may add other cases In three of the transfused cases with blood volumes below 70 per cent and low blood pressure it is known that blood pressure was low before transfusion was begun Moreover, there are seven others without blood volume measurements not included in Table 6, six with very large and one with large wounds, who may all be presumed to have lost much blood All were seen ½–3 hr after wounding, none had been transfused but all required large transfusions and it is reasonable to assume that in all of them blood volume was well below

TABLE 6

Wound size, blood loss and blood volume related to circulatory state
51 Italian patients with limb injuries

Patient	Wound size	Time after injury (hr)	Blood loss (per cent predicted normal blood volume)	Blood volume (per cent predicted normal)	Blood pressure (mm Hg)	Pulse rate (per min)	Face colour	Extremity temperature	Remarks
1	Small	4	Under 5	118	130/100	72	Good	Warm	A
14	"	9½	" 5	112	160/70	64	"	Cold	
7	"	18½	" 5	112	110/75	84	"	Warm	
6		1¼	" 5	107	140/60	88	"		
37	Moderate	2	" 5	106	160/50	90	"		
[illegible]	Small	18	" 5	105	120/70	60	"	"	A
9	"	7	" 5	104	140/80	80	"	"	
12	"	22	" 5	102	150/90	88	—		
41	Moderate	5	5	102	135/80	84	Pale	Cold	
18	Small	15	20	100	112/90	76	Good	Warm	
90	Large	24	?	98	70/40	60	Pale		Tr
35	Moderate	19¼	15	98	140/80	92	—	"	
77	Large	6¾	35	94	165/90	168	Pale	Warm	Tr A
3	Small	6½	5	93	130/70	60	Good	"	
24		8¼	25	90	115/70	88		"	
66	Moderate	6½	15	90	130/60	80	"	Cold	A
40	"	22½	25	89	130/80	100	"	"	A
89	Large	14	40	85	130/80	120	"	Warm	Tr
49	Moderate	53	35	84	130/70	128	Pale	"	A
25	Small	10¾	45	84	75/40	96	—	Cold	Tr
74	Large	3¾	25	83	110/60	90	Pale	Warm	
20	Small	10	20	82	155/90	100	Good		
58	Moderate	15½	45	81	140/95	124		Cold	Tr A
88	Large	1	30	80	135/80	76	Pale		
104	Very large	3½	25–30	80	115/80	100	—	"	
60	Moderate	8	25	79	140/90	120	Pale	Cold	A
43	"	4¾	45	78	116/65	140	Good	Warm	Tr
39	"	17¼	45	75	125/80	120		Cold	A
46	"	5½	40	75	115/70	126	Pale		A
57	"	1½	40	75	110/70	128	"		
51		6¼	C25	C75 ?	120/70	108		Warm	
86	Large	6½	45	74	110/85	120		Cold	
76	"	5½	40	74	90/65	124	"	"	
95	Very large	4	40	72 ?	115/90	108		"	Tr
33	Moderate	1½	C40	C72	155/70	[illegible]	"	Warm	
23	Small	10	50	71	125/65	112	"		
79	Large	8	40–45	70	130/80	106		"	
44	Moderate	4	35	70	135/90	90	Good		
98	Very large	8½	60	67	55/30	122	Pale	Cold	Tr
55	Moderate	4	40	67	140/90	112		"	
83	Large	7	55	64	130/80	112	"		Tr
99	Very large	5¾	45	61	95/70	112		"	
45	Moderate	5½	55	60	85/70	112	"		
78	Large	3½	50	60	70/60	128			
106	Very large	7¾	C60 ?	C60	50/25	140			
15	Small	9	C60 ?	C60 ?	50/30	120			
73	Large	5	C45 ?	C60 ?	80/55	116		Warm	
93	Very large	7½	60	54	160/60	160		Cold	Tr during rigor
101	"	2¼	C60 ?	C50 ?	50/40	144			Tr
110	" "	1½	C60 ?	C50 ?	35/?	?			Tr no radial pulse
53	Moderate	6½	C50–60	C48	70/50	100			

A = Injection of atropine or papaverine with scopolamine within the previous hour
Tr = Prior transfusion
Values obtained by back calculation are marked by C, those thought less reliable than the others are indicated by ?

TABLE 7

Blood volume related to circulatory state untransfused Italian patients with limb injuries

Blood volume (per cent normal)	Blood pressure (mm Hg)				Pulse rate (per min)				Face colour			Finger temperature		
	Over 140	140–100	Under 100	*Total*	Under 70	70–99	100 and over	*Total*	Good	Pale	*Total*	Warm	Cold	*Total*
Over 95	3	8	0	*11*	2	9	0	*11*	8	2	*10*	8	2	*10*
95–80	1	8	0	*9*	1	4	4	*9*	5	3	*8*	4	5	*9*
79–70	1	9	1	*11*	0	2	9	*11*	2	8	*10*	4	6	*10*
Under 70	0	1	7	*8*	0	0	8	*8*	0	8	*8*	1	7	*8*

TABLE 8

Blood volume related to circulatory state untransfused patients with limb injuries (Home Series)

Assumed blood volume (per cent normal)	Blood pressure (mm. Hg)				Pulse rate (per min)				Face colour			Finger temperature		
	Over 140	140–100	Under 100	*Total*	Under 70	70–99	100 and over	*Total*	Good	Pale	*Total*	Warm	Cold	*Total*
Over 95	5	10	3	*18*	7	10	1	*18*	10	7	*17*	11	7	*18*
95–80	10	23	7	*40*	11	21	5	*37*	17	17	*34*	17	18	*35*
Under 80	2	16	44	*62*	6	20	34	*60*	7	40	*47*	14	27	*41*

70 per cent normal Blood pressure was unrecordable in three and not over 80 in the others

It may be concluded that in instances of limb injury in previously fit young adults, seen within 12 hr of wounding and not transfused, a blood volume reduced by haemorrhage to below a critical level of 70 per cent of the predicted normal is associated with a blood pressure of below 100 mm Hg

Table 8 shows that for the Home Series there is a similar relation between blood volume and blood pressure Low blood pressure is the rule with a blood volume below 80 per cent normal, how much below, the data do not show Whether or not the critical level of blood volume is the same for the older patients in the Home Series as for younger military cases is not determined, but it is unlikely to be lower than 70 per cent normal

There are, however, in the Home Series a number of cases in whom the blood volume was judged to be 80–95 per cent, and even a few with blood volume above 95 per cent, in whom the blood pressure is below 100 There are none similar in the Italian Series These cases are not to be accounted for by errors in assessing blood loss They indicate the existence of subsidiary factors, other than the chief one of haemorrhage, that may reduce blood pressure in the initial state

A second point that emerges from the tables is that in both series hypertension (blood pressure over 140) is uncommon with blood volumes below 80 per cent normal Thus of the 5 untransfused Italian cases with hypertension only 1 had a blood volume below 80 per cent, and in this instance it was not much below, 72 per cent Of the 17 similar Home cases, the blood volume was judged to be below 80 per cent in only 2, how much below is unknown

OTHER CIRCULATORY FEATURES

Circulatory Patterns

The other features specially observed, pulse rate, face colour and finger temperature, tend to combine with each other and with blood pressure to form certain patterns To display these the cases in Table 9 are divided into three groups according to the level of systolic blood pressure, as normal (100–140 mm Hg), raised (over 140) and low (under 100) These groups are subdivided according to (i) pulse rate, as normal (70–99), slow (under 70) and fast (100 or over), (ii) face colour, as pale or good, (iii) finger temperature, as warm or cold

Though the combinations are various and grade into each other, a number of distinctive patterns are to be recognized, of which some are more common than others

a *With normal blood pressure* (i) most commonly (21 cases out of 91) all features are normal, (ii) one third (32 out of 91) have a fast pulse, 44 per cent of them (13) having good face colour and warm fingers and (iii) an equal proportion (13) a pale face and cold fingers

b *With raised blood pressure* the pulse rate is more often (16 cases out of 21) normal, but may be fast or slow Other features are variable, (i) the most common picture (9 cases) is good face colour and warm fingers, but (ii) the next most common is a pale face and cold fingers (5 cases)

TABLE 9

The interrelation of circulatory features

Blood pressure (mm Hg)	Pulse rate (per min)	Face colour: Good		Face colour: Pale	
		Finger temperature: Warm	Finger temperature: Cold	Finger temperature: Warm	Finger temperature: Cold
Raised (over 140)	under 70	*1+2	—	—	0+2
	70–99	1+2	0+3	2+1	0+2
	over 99	1+2	—	1+0	0+1
Normal (140–100)	under 70	4+5	0+1	0+1	0+4
	70–99	11+10	1+3	5+4	5+5
	over 99	12+1	2+1	2+1	13+0
Low (under 100)	under 70	—	—	1+0	0+5
	70–99	1+0	—	0+3	1+6
	over 99	1+1	0+1	1+2	22+14

*The numbers of Italian cases are shown in roman type and those of English cases in italic

c *With low blood pressure* the face is almost invariably pale (55 cases out of 59) Accompanying this, (i) very commonly (36 cases) the pulse is fast and the fingers cold, (ii) much less commonly (12 cases) the fingers are cold, but the pulse is slow or normal, (iii) occasionally (5 cases) the pulse is fast or normal and the fingers are warm

Relation to blood loss In Tables 6, 7, and 8 (pp 16 and 17) are shown circulatory features related to blood loss for those cases of both series in which all features were noted It is evident that pallor and coldness become more frequent and pulse rate quickens as blood loss increases and blood volume diminishes Thus in the Italian Series blood pressures of at least 100 with, in most cases, normal pulse rate, good face colour and warm fingers, are associated with near-normal blood volumes With blood volumes between 95 and 80 per cent normal the pulse rate may or may not be fast, the face may or may not be pale and the fingers may or may not be cold With blood volumes between 80 and 70 per cent normal, though blood pressure is normal, most cases have fast pulses, pale faces and cold fingers With blood volumes reduced below the critical level of 70 per cent at which blood pressure falls, tachycardia, pallor and coldness are present almost without exception In the Home Series similar relations between blood volume and circulatory pattern are found

We may conclude that, of the circulatory patterns enumerated above, the normal combination of normal blood pressure and pulse rate, good face colour and warm fingers (*a* (*i*)) *is found* chiefly among those who have lost little or no blood and whose blood volume is normal or nearly so Of the others, that of low blood pressure, fast pulse, pale face and cold fingers (*c* (i)) is the pattern of greatest importance, being the expression of large blood loss,

sufficient to reduce blood volume below 70 per cent normal A smaller haemorrhage, reducing blood volume to between 70 and 80 per cent normal, results in the pattern of normal blood pressure, fast pulse, pale face and cold fingers (*a* (iii)) The remaining patterns are the expression, not of blood loss alone, but of blood loss combined with the other factors now to be discussed or of these other factors alone

OTHER FACTORS MODIFYING CIRCULATION

Other factors recognized to affect the circulation in these patients are emotional and sensory stimuli such as pain, fright and apprehension, exposure to heat or cold, treatment before coming under observation, and age Differences in the incidence of these factors are responsible for differences in the circulatory features between the two series

The Home Series includes many cases older than any in the Italian, so that in general pulse rate is slower at all levels of blood pressure (Table 9)

From what has been said earlier, it will be clear that in the Italian Series the interval between wounding and observation was in most cases sufficiently long to allow the effects of the sensory and emotional stimuli which arose at the time of wounding to subside Treatment during this interval was such as to allay pain, fear and apprehension and to promote warmth Most cases when first seen appeared emotionally normal, only a few, and those mostly prisoners of war, were apprehensive and only a few appeared to suffer pain, mainly those injured in the neighbourhood and admitted direct to hospital Most of them were warm and some were hot and sweating The majority of the Home Series, on the other hand, were seen soon after wounding in colder weather and had received little or no treatment Many were in pain, frightened by their experience and apprehensive of their state Many were cold, and some shivered

In normal subjects exposure to cold cools the extremities, slows the pulse and slightly raises the blood pressure Warmth, on the other hand, heightens facial colour, warms the extremities, increases pulse rate and slightly lowers the blood pressure Emotional stimuli in some instances considerably raise the blood pressure, increase pulse rate, pale or flush the face and cool the extremities, in others, while paling the face and cooling the fingers, they may lower blood pressure and slow the pulse

The effects of each of these stimuli cannot be traced in detail, it is however clear that they disturb the normal circulatory pattern in the absence of blood loss and modify the effects of haemorrhage in our patients Thus, for example

(1) In the Italian Series most of those with normal blood pressure and little blood loss showed the normal circulatory pattern, but in the Home Series a considerable number of such patients were pale and cold

(2) In both series, though particularly in the Home, some patients showed raised blood pressures associated not only with normal or nearly normal blood volumes but also with volumes reduced to between 95 and 80 per cent, and in two of the Home Series to below 80 per cent

(3) In both series, a few of the patients showed the unusual association of warm extremities and either a well-coloured or a pale face with a low blood

pressure and greater blood loss Patients of the Italian Series displaying this pattern were all seen in hot weather Information about the Home Series is incomplete in this respect but at least half the patients had been over-warmed before being seen

(4) In the Home but not in the Italian Series, among those with low blood pressure is a number of patients with the usual pale faces and cold extremities but also, and unusually, a slow pulse rate (the vasovagal syndrome) In most instances this circulatory pattern was associated with a blood loss assessed as negligible or under 20 per cent, in a few the loss was assessed at over 20 per cent, but it is not known how much over

ADDITIONAL SIGNS

In addition to pallor and coolness of the skin, other signs also indicate vasoconstriction in these patients The *radial artery* becomes narrowed, sometimes so much that its pulse is impalpable even though blood pressure is not low The *superficial veins* are also narrowed and may be so constricted that it is difficult to insert a needle and impossible to withdraw blood Great constriction of artery and veins can be produced by exposure to cold alone Both were commonly but not invariably constricted in patients losing much blood, even in warm weather Though the forearm veins were greatly constricted, the external jugular veins often remained little constricted and filled above an obstructing finger, thus offering a site for the withdrawal or transfusion of blood when the forearm veins were unusable The facial pallor often contrasted with the *colour of the lips*, which, emphasized by the surrounding pallor, sometimes appeared good even when 40–50 per cent of the blood was estimated to have been lost Pallor of the lips we believe to be a sign of great blood loss It was noted in the initial state in six patients, in three of the Italian Series blood loss was estimated as 40, 55 and over 60 per cent, while in the other three it was unmeasured, but the wounds were very large *Cyanosis* was not a conspicuous feature with any degree of blood loss When present, it was usually no more than a slight blueing of the lips and extremities attributable to a reduced local circulation A more evident cyanosis in the initial stages was noted in two patients only, where respirations were laboured and rapid, and extensive haemorrhages and many fat emboli were found in the lungs after death

Sweating in the initial state, and apart from warmth, was seen mainly in patients with hypotension It was associated with both the vasovagal syndrome and much blood loss *Nausea and vomiting* were uncommon, morphine appeared the usual provoking cause, but they also sometimes occurred in those presenting the vasovagal syndrome and in those losing much blood A large proportion of all patients complained of *thirst* either on their own initiative or when asked, but an urgent thirst, causing the patient repeatedly to call for water and to drink avidly, was seen only in those losing much blood The *rate and depth of respiration* were not in most cases notably altered Sighing respirations were associated both with the vasovagal syndrome and with much blood loss Air hunger was seen in one patient of the Italian Series, blood loss and volume were both estimated at about 60 per cent of

predicted normal blood volume His respirations were deep and about 50 per min and he complained that he could not get his breath The air hunger was relieved by transfusion

Two types of *restlessness* were distinguished One, in which the movements seemed directed to easing the pain of the injured part, was seen in many patients of the Home Series, but in only a few of the Italian, whose pain had been relieved In the other type the movements, chiefly a tossing about of the arms and head, were apparently the expression of a general and almost intolerable discomfort This great restlessness was noted in only eight patients (four in each series), all of whom had lost much blood In three of the Italian Series, blood loss was estimated to be at least 60 per cent, two of them had a blood volume of less than 50 per cent

Motor power was remarkably good even in those losing much blood We were often astonished at the strength displayed by such patients, as shown by the force required to restrain the restless or to wrest a cup from the avidly thirsty Another striking feature of all cases, even those losing much blood, was their entire consciousness and *mental alertness* Only two of all the patients of both series who had lost much blood were confused, and four unconscious, all became mentally normal after transfusion Loss of consciousness is known to be associated with the vasovagal syndrome, but none of our patients displayed it *Apathy* was rare and seemed due to large doses of morphine Except as a result of morphine, we did not meet with *insensibility to pain* Patients dying from blood loss have complained of apparently minor discomforts, for instance that a hot water bottle was too hot or that the sphygmomanometer cuff hurt the uninjured arm.

COMMENT

Two clinical pictures of chief importance emerge from what has been described above They are alike in many respects, but one is restricted to those who have bled greatly while the other may occur even when no blood is lost

The first picture is characterized by very low blood pressure, below 70 mm Hg, impalpable pulses, very rapid heart rate and cold extremities with constricted veins To this may be added great restlessness, dyspnoea, sweating, nausea and vomiting This picture was seen in cases of both series and was associated usually with large and very large wounds and always, so far as our observations go, with great blood loss and blood volumes well under 70 per cent normal

The second picture is characterized also by low blood pressure and impalpable pulses, pallor and cold extremities, but by a slow heart rate, and though yawning, sighing respirations, sweating, nausea and vomiting may be added there is no great restlessness nor dyspnoea This picture was seen only in patients of the Home Series soon after injury and was associated especially with small wounds and little or no blood loss It presents the combination of signs commonly termed the vasovagal syndrome, which is well known to be provoked by emotional and sensory stimuli alone

TRANSFUSION REACTIONS AND THEIR EFFECT

About a quarter of the patients of the Italian Series received transfusions before we saw them Apart from their action in increasing blood volume, the blood, serum and plasma transfused, both in Italy and at home, frequently had marked pharmacological effects Since these transfusion reactions may influence the initial clinical picture of the patient, they are now described

Typically a severe reaction starts with a phase of cutaneous vasoconstriction which is followed sooner or later by a phase of vasodilatation

In the initial stage the face becomes pale and the extremities cold The radial pulse narrows and may become impalpable, while the forearm veins constrict until it is very difficult or impossible to withdraw blood The venous constriction slows or even interrupts the transfusion, which may have to be forced in under pressure and cause pain in the transfused limb The blood pressure is increased, and may rise to 160 or more, the pulse rate also is increased and may reach 140 or more The patient becomes restless and excited shivers violently and may yawn repeatedly between the bouts of shivering Breathing becomes deep, often increasing in rate and, because of the shivering, becoming irregular The patient may groan and complain of pain in the back and limbs Because of the diminished heat loss caused by constricted vessels and the increased muscular movements, body temperature rises After a varying period, sometimes an hour or longer, this stage is followed by a period of vasodilatation in which overactivity and restlessness have passed off and the patient is at peace, blood pressure and pulse rate fall, although pulse rate may remain over 100 for some time Cutaneous vasodilatation is associated with these changes and is sometimes very marked The face is flushed and the pulse bounding, the extremities are warm or hot and the superficial veins wide Sweating is profuse

With less severe reactions shivering and other signs may be absent, the reaction being only a rise of blood pressure, some increase of pulse rate and a complaint of feeling ill Severe transfusion reactions are more liable to develop if a transfusion is given rapidly than if it is given slowly

Two points about the phase of constriction require notice here One is that patients transfused before they are seen by the surgeon may be found to be pale and to have cold extremities and a very rapid pulse, 140–160 per min If it is not recognized that this state may have been caused by a previous transfusion, the blood loss may be overestimated and the patient wrongly thought to be in a more dangerous state than in fact he is The second is that patients who when first seen are in a state of circulatory collapse may show this vasoconstrictor response even to small transfusions which are insufficient to increase blood volume materially The blood pressure may rise to normal or hypertensive levels which may be maintained for some time, so that to the inexpert, judging by blood pressure alone, the patient may seem adequately resuscitated In one case (*I* 93), with a measured blood volume of 54 per cent, the blood pressure was raised from 75/? to 160/60 and the pulse rate from 148 to 160 in the course of a rigor during the transfusion of about a quarter of a bottle of blood In these patients, however, the persistence of vasoconstriction and the rapidity of the pulse, together with the onset of shivers, restlessness and often deeper breathing, should, if the amounts of blood loss associated with circulatory collapse are known, prevent errors of judgment leading to undertransfusion with its dangers to the patients' further course and recovery

Course Before Operation

INTRODUCTION

In the preceding section the circulatory state of the patients when they were first seen has been considered The changes in their state up to the time of *operation are now* described, and the factors responsible for them are discussed A note is needed about treatment during this period, which was *slightly shorter in the Italian than in the* Home Series (Table 11, p 38)

The Home cases were usually undressed and put to bed, the battle casualties *of the Italian Series remained clothed on their stretchers* until operation Their wounds were dressed or redressed and splinted if necessary Those patients who were not thought to need resuscitation were left to rest till operation, they were supplied with fluids to drink and allowed to smoke if they wished *Pre-operative medication with atropine, etc* was *given to the* majority, sometimes soon after admission

At home, in the early days of the air raids, the usual treatment given to those judged to be "shocked" was rest, often in the head-down position, morphine (usually ¼ gr) and warmth Warming was carried out by hot blankets, hot water bottles or an electric cradle In addition to fluids by mouth, intravenous or rectal salines were sometimes given, often oxygen was administered, sometimes also such drugs as adrenaline or coramine Transfusion of blood or plasma was resorted to usually only after other measures had failed to relieve "shock", and was then given *slowly and in small amounts*, but small transfusions were sometimes given earlier if there were signs of gross and continued bleeding Patients thought to be very severely "shocked" were sometimes left clothed and almost unexamined until they were thought to have recovered sufficiently Those judged to be "moribund" were put aside to die

As the war progressed treatment changed, particularly in the direction of greater emphasis on transfusion In Italy patients were examined and wounds treated early Transfusion of blood, plasma or serum was given earlier and more freely, it was often used prophylactically Further details are given later (p 104)

CIRCULATORY CHANGES

In following the circulatory changes that occur before operation the systolic blood pressure is the most useful sign For descriptive purposes the patients are divided into the three groups, with raised, normal and low blood pressures, that have already been seen to be associated with particular circulatory patterns and with degrees of wound size and blood loss

Before operation the circulation is influenced by several factors, e g further haemorrhage, nervous stimuli and any treatment given, the effect of these factors on the circulation is determined mainly by the level of initial blood *volume* Where blood volume is above the critical level of about 70 per cent normal, circulation is generally maintained until operation, but the nearer the blood volume is to that level the more liable is hypotension to

develop In general, also, the low blood pressure of those with a blood volume below that level can only be quickly restored by transfusion

Patients with Hypertension
(*Blood pressure over* 140, 23 *cases*—17 *Home*, 6 *Italian*)

Hypertension was a not uncommon sequel to limb injuries and was usually associated with a normal or slow pulse rate, cutaneous constriction or dilatation, small or moderate wounds and blood volumes within 20 per cent of the predicted normal

Most patients were not transfused Under the influence of rest, warmth and morphine, their general course was a return to a more normal circulatory state, as shown by a fall of the blood pressure to normal levels, and a release of any vasoconstriction that had been present. In most cases the blood pressure was normal and pallor had gone or lessened before operation, but occasionally the pressure was again raised by suitable stimuli Hypotension developed in only one case, one of the few judged to have lost over 20 per cent of his blood, who was overheated by hot water bottles and became flushed, hot, sweating and restless

The course before operation thus provides further evidence that in these cases the hypertension is the result, not of blood loss, but of emotional and sensory stimuli associated with the injury

Patients with Normal Blood Pressure
(*Blood pressures* 100–140, 107 *cases*—49 *Home*, 58 *Italian*)

In the Home Series little of note occurred in patients assessed as losing less than 20 per cent of their blood (blood volume probably 80 per cent or more), their wounds were small or moderate Most of them were warm and of good colour and had normal pulse rates Those who were cold became in time warmer and more comfortable, pallor, shown by less than half, decreased or gave way to a good colour Blood pressures remained unchanged or fell slightly, but not to below 100 Only one case was transfused prophylactically, because his pallor persisted and his blood pressure fell to 100, although his pulse rate remained at 70–80 A few showed transient falls of blood pressure of the vasovagal type, apparently in response to painful stimuli

In those assessed as having lost 20 per cent of their blood (blood volume probably below 80 per cent but not below 70 per cent) there was more to note For the most part their wounds were moderate and they were pale and cold, in about a third the pulse rate was fast (over 100) Only half (including some transfused prophylactically) maintained blood pressures above 100 until operation The data are incomplete, but in most of the others the fall was associated with renewed or continued bleeding and accompanied by an increase of the pulse rate and cutaneous vasoconstriction Blood pressure was in all cases restored to normal before operation, in all but one by transfusion In the untransfused case the fall of the blood pressure, accompanied by cutaneous vasodilatation, was apparently due to overheating added to the previous blood loss

Over a period of 2 hr while she (*Case H 7*) was lying under an electric cradle, she became uncomfortably hot and restless, her blood pressure fell gradually from

135/90 to 95/60 and her pulse rate rose from 80 to 90. When heating was withdrawn she became cooler and vasodilatation subsided, the blood pressure rose but remained at a lower level than before, 105/65, with a pulse rate of 85.

Judging by later experience, many of these patients ought to have been given prophylactic transfusions soon after admission, in which case the fall of blood pressure would in all probability have been prevented.

Of the Italian Series, only about one third were not transfused before operation. Most of these untransfused patients had small wounds, a good colour and a normal pulse rate. Blood volume, measured in nine, was above 80 per cent normal in seven and between 70 and 80 per cent in two. Circulation was maintained in all until operation.

About a quarter of the patients of the Italian Series had already been transfused and in most of them transfusion was continued; in the remaining cases it was begun soon after initial observation. The need for transfusion was judged mainly by wound size, which was moderate in most. Many of the patients were pale and in about half the pulse rate was fast. The blood volume, measured in 11, was between 70 and 80 per cent normal in 8 and over 80 per cent in 3. Circulation was maintained until operation, except in two cases in whom, before transfusion was begun, the blood pressure fell below 100 and the pulse rate increased when the patient was turned on one side to allow examination of his wounds. One of them shows how very small stimuli can cause a fall of the blood pressure in patients with a blood volume near the critical level.

Case I 23 had been steadily oozing blood over 20 hr. from a compound fracture of the maxilla, and the disorganization of his soft palate had made breathing difficult. *During the course of blood volume estimation his blood pressure, which had been 125/65, fell to 60 and later to 70, and his pulse rate, which had been 112, rose to 140. During this time he lost little further blood and the blood pressure fall seemed to be related to turning him on his side and to general discomfort. The blood pressure was restored to normal by the slow transfusion of two bottles of blood over about 3 hr. At the time of the blood pressure fall his blood volume was 71 per cent of the predicted normal.*

In both series the patients given prophylactic transfusions usually received one or two bottles of blood, plasma or serum. This transfusion caused no obvious change in some, others became warmer and of better colour, in a few the pulse rate slowed. Transfusion reactions were common and in most cases the vasoconstriction and increase in blood pressure and pulse rate persisted till operation.

Patients with Hypotension

(*Blood pressure under* 100, 91 *cases—54 Home, 37 Italian*)

In both series the great majority of patients who had hypotension also had pale faces and cold extremities, almost all of the Italian Series and most of the Home Series falling into this category; most had a fast pulse, but in a few of the latter the pulse rate was slow. Their wounds were mainly moderate or large. Most of the Home Series were assessed as having lost over 20 per cent of their blood. In 12 of the Italian cases the blood volume was measured or calculated, and in all but 2 it was under 70 per cent normal.

In Italy almost all such cases were transfused before or soon after being seen At home, none were transfused before being seen and in the majority transfusion was delayed until the other therapeutic measures already mentioned had been tried The period of delay ranged from ½ to 12 hr, but was 1–2 hr in the great majority We had, therefore, an opportunity of seeing whether or not these other measures were effective

Only a few of the patients of the Home Series recovered without transfusion All of them had small wounds and all but one were assessed as having lost less than 20 per cent of their blood, most had a slow pulse rate and presented the vasovagal syndrome, but in some the pulse rate was normal The rise of the blood pressure to normal levels was usually accompanied by an improvement in colour and an increase of pulse rate The following examples illustrate recovery and show, moreover, that the hypotensive state may be renewed when suitable stimuli are applied

In two patients prompt recovery was produced by raising the foot of the bed One of them, *very pale, cold, sweating and nauseated, with a blood pressure of 60/?* and a barely palpable radial pulse (40 per min at the carotid) began to improve as soon as the bed foot was raised * Eight minutes later the blood pressure was 100/65 and the pulse of good volume, at 64 per min, sweating had ceased and nausea abated, though she remained pale for some time In two others similarly treated about an hour elapsed before the blood pressure began to rise

In one case, after initial recovery the blood pressure fell steeply from 130/80 to 90/60 and the pulse slowed from 80 to 68 during attempts to introduce a needle into a vein, she recovered from this in 15 min

In another patient recovery followed relief of severe pain by morphine When pain was later renewed by manipulation of the injured arm the blood pressure fell again, the radial pulse narrowed and slowed, the skin paled and cooled, and sweating recurred, he recovered within 30 min

In another patient the gradual rise of blood pressure over a period of 3 hr was twice interrupted by a transient fall, on one occasion during manipulation of the injuries

The remainder showed little or no improvement They included all those with a fast pulse rate and a few with slow or normal pulse rates, most were assessed as having lost over 20 per cent of their blood Until transfused most of them remained unchanged, in a few the blood pressure rose a little, in others it fell lower and even became unmeasurable The majority responded well to transfusion

Hence it may be concluded that few of those patients who when first seen have a low blood pressure, and in particular those in whom this is associated with more than a little blood loss or with more than small wounds, will show a return to normal blood pressure without transfusion

RESPONSE TO TRANSFUSION

Introduction

The transfusion fluids available at home were mainly stored blood and liquid plasma and in Italy were stored blood and reconstituted dried plasma and serum

* In almost all injured patients with a low blood pressure raising the bed foot causes a speedy rise of 5–10 mm Hg which may not be maintained

In both series most of the patients with hypotension recovered or improved greatly when transfused with any of these fluids Improvement, judged not only by the rise of the blood pressure but also by subjective changes, was usually pronounced within an hour or two of the beginning of transfusion In some it was dramatic in its rapidity, in others delayed In the majority the rise of blood pressure was accompanied, not by a slowing of the pulse rate, but by an increase of 10–40 beats per min, which was maintained till operation The colour of the face and the temperature of the extremities were affected in various ways In some vasoconstriction was released, the skin becoming warmer and pinker, the pulse wider and the veins relaxed, but in many cases pallor and coldness persisted in greater or less degree till operation Transfusion reactions were frequent with all the transfusion fluids, particularly when transfusion was rapid

The circulatory changes brought about by transfusion are complex, and are determined by the interaction of a number of factors The most important of these are the initial blood volume, the volume, composition and pharmacological properties of the transfused fluids and the rate at which they are given, and the time after injury at which transfusion is begun It is not always possible to distinguish the effects of the individual factors Thus it is impossible to separate clearly the effects of the volume of the fluid from those of its pharmacological properties The effects of amount, rate and time of beginning transfusion are best seen in those previously losing much blood, if such patients are to recover, it is of first importance not only that the transfusion should be adequate in volume but also that it should be begun without delay and given rapidly

We now discuss the effects of the various factors individually

Volume of Transfused Fluid

Experience of the Italian Series shows that the blood pressure is restored to and remains at normal levels or above when the volume of fluid transfused is adequate to raise the blood volume to near the critical level of 70 per cent normal or above it The following cases are illustrative

Case I 73 was seen 5¼ hr after receiving large injuries to both legs He was pale though not cold, his blood pressure was 80/55 and his pulse rate 116, his blood volume was about 60 per cent normal

★Two bottles of blood were transfused over 1¼ hr Shortly after beginning the second bottle the blood pressure reached 105/75 and the pulse rate 120, at the end of this bottle the blood pressure was 120/70, he was pale and cold and the forearm veins were constricted, the blood volume was calculated to be 75 per cent normal ★ Transfusion was continued and the patient sent to operation

Case I 53, with moderate wounds of the legs, lost much blood from a severed femoral artery

Seen at 6 hr he was pale cold and thirsty and his veins were constricted, his blood pressure was 70/50, his pulse rate 100, his blood volume was calculated to be 48 per cent normal

★Transfusion of three bottles of serum over ¾ hr raised the blood pressure to 100/40 After a fourth bottle, given over 2 hr, the blood pressure was 120/70 and the pulse rate 120, he was then a good colour and warm and his veins were relaxed and full, the blood volume was measured and found to be 77 per cent normal ★ Transfusion was continued and the patient was sent to operation

However, although the blood pressure was restored to normal by transfusion, and although in some patients the amounts of transfusion given were thought sufficient to replace lost blood, yet the normal circulatory pattern was seldom restored Pallor, coldness and tachycardia persisted till operation in many patients This was due to two factors, the fact that the volume transfused was often inadequate to raise blood volume to much above the critical level, and the pharmacological effects of the transfused fluids

The fluids were supplied in pint bottles, those of blood and plasma contained nominally 540 ml and those of serum about 500 ml It was commonly assumed that the transfusion of a bottle would increase the blood volume by the amount of the contents But it will be seen from Part IV that this assumption is false A bottle of blood may be expected to increase the blood volume not by 540 ml, i e approximately 10 per cent of the average normal blood volume, but only by 430 ml, i e approximately 8 per cent, and that only if all the protein administered remains in the circulation and the red cells are not rapidly destroyed Similarly a bottle of plasma of 400–540 ml and one of serum of about 500 ml may be expected to increase the blood volume by about 300 ml and 500 ml respectively, or approximately 5 and 9 per cent of the average normal blood volume

Because of this error and also because at the bedside blood loss was often underestimated*, many of the patients who had lost much blood reached operation with a blood volume below normal and often not far above the critical level

In the Italian Series six patients previously untransfused had blood volumes estimated as 60–65 per cent They received amounts of transfusion equivalent to 6 per cent (*Case I* 99, blood volume 61 per cent), 17 per cent (*Case I* 73, blood volume 60 per cent), 18 per cent (*Case I* 78, blood volume 60 per cent), 26 per cent (*Case I* 45, blood volume 60 per cent), 28 per cent (*Case I* 106, blood volume 60 per cent) and 31 per cent (*Case I* 15, blood volume 60 per cent)

Two others, previously untransfused, whose blood volumes were calculated to be about 50 per cent of the predicted normal, received transfusion equivalent to 18 per cent (*Case I* 101) and 38 per cent (*Case I* 110) of their predicted normal blood volumes In the last case further blood was lost by haemorrhage during this transfusion

There are three patients whose blood volumes were measured after previous transfusion, *Case I* 98 (blood volume 67 per cent) was then given further transfusion equivalent to 6 per cent of his normal blood volume, *Case I* 83 (blood volume 64 per cent) 7 per cent more and *Case I* 93 (blood volume 54 per cent) 16 per cent more

Of three patients whose blood volumes were estimated after transfusion to be about 80 per cent, two (*Cases I* 43 and 58, blood volumes 78 and 81 per cent) were then sent to operation, the third (*Case I* 95, blood volume 72 per cent) was given two more bottles of plasma, or a further 11 per cent of his normal blood volume

In the Home Series four patients had bilateral leg injuries with total tissue damage of 3–5 hands and systolic blood pressures of about 80 From their injuries and clinical state it can be reasonably judged that their initial blood volumes were of the order of 60 per cent of their normal Before operation they were given amounts of transfusion equivalent to about 14 per cent (*Case H* 110), 21 per cent (*Case H* 105), 22 per cent (*Case H* 102) and 35 per cent (*Case H* 115) of their normal blood volumes

Four other patients, also with bilateral leg injuries, had tissue damage of over 5 hands and initial blood pressures of not more than 60 Their initial blood volumes may

* The results of blood volume measurement were usually not available in time to guide treatment

well have been of the order of 50 per cent normal or less They were given amounts of transfusion equivalent to about 12 per cent (*Case H* 113), 18 per cent (*Case H* 117) and 30 per cent (*Case H* 116) of their normal blood volumes

It follows, therefore, that the persistence of tachycardia and vasoconstriction after the restoration of blood pressure to normal by transfusion can, in part at least, be accounted for by the fact that the blood volume, though raised above the critical level, was seldom restored to normal or nearly normal levels

Pharmacological Properties of the Transfused Fluids

Transfusion reactions, the expression of the pharmacological properties of the transfused fluids, were common, and often considerably modified the circulatory state All grades were seen between severe reactions, such as that described on p 23, and mild ones in which the patient did *not* shiver and the circulatory changes of the constrictor phase were no more than a slight pallor and cooling of the skin, a small increase of the pulse rate and little or no rise of the blood pressure It is clear, therefore, that the vascular changes of the constrictor phase may more or less modify those brought about by the increase of blood volume by the transfused fluids Thus when the blood volume is raised from below to not far above the critical level, though the blood pressure becomes normal, pallor, coldness and tachycardia tend to be increased, when it is raised well above the critical level, vasodilatation and slowing of the pulse rate tend to be prevented *Case I* 104 (p 55) illustrates the persistence of pallor and tachycardia when the blood volume is restored to normal

Case I 93 (p 52) shows how during a severe reaction, although the blood volume may remain below the critical level, the blood pressure may be raised from hypo- to hyper-tensive levels

If before operation the constrictor phase of the reaction is replaced by the dilator, the associated vascular changes may also modify those due to the increase of the blood volume In the dilator phase the blood pressure falls and the pulse rate follows, though more slowly The cutaneous vessels are relaxed, sometimes greatly These changes account for the unusual circulatory patterns occasionally met with in the later stages of transfusion or after it has stopped Thus in some instances when blood volumes were near normal, although the blood pressure was *normal*, the usual good face colour, warm fingers and normal pulse rate were replaced by a flushed and hot skin and a fast pulse On occasion the blood pressure was lower than normal, as *Case I* 90 illustrates (Table 6, p 16) On occasion also, as in *Case I* 53 quoted above, when the blood volume was raised only a little above the critical level the usual pallor and coldness were replaced by good colour and warm extremities, although the blood pressure was normal and the pulse rate, as usual, fast

Time of Beginning Transfusion

Experience of the Home Series shows that in the majority of patients in whom hypotension was allowed to persist for an hour or two blood pressure could be restored by transfusion For example

Case H 9, a man aged 26, was admitted ½ hr after having cut his throat The trachea was severed and there had been much blood loss He was unconscious and pulseless, had an unmeasurable blood pressure, and seemed almost dead He was put to bed, given morphine ¼ gr and warmed ★At 1½ hr the blood pressure was 40/? and the pulse rate 106 Since no further improvement occurred transfusion was started at 2¼ hr and the first bottle of blood given in ¾ hr After this the blood pressure was 65/30 and the pulse rate 106 The second and third bottles were given in 1 and 2¼ hr respectively, he was then conscious and rational and his pulse rate was 100 No more transfusion was given At 8½ hr the blood pressure was 100/60 and the pulse rate 110, at 12 hr they were 120/80 and 100 At 13½ hr the haemoglobin was 55 per cent At 15½ hr the blood pressure was still 120/80 and the pulse rate still 100, and at 32 hr they were substantially unchanged ★ No further information is available

Later experience made it clear, however, that in such instances of great blood loss and marked circulatory collapse delay in beginning transfusion was liable to result in early death In the following example it is probable that the half hour's delay was responsible for death

Case I 103, an Italian peasant woman aged about 40, was seen 2½ hr after treading on a mine Her left foot was blown off and most of her left leg shattered She had a huge laceration of the posterior aspect of the right calf and many small lacerations and contusions elsewhere The total tissue damage was estimated at necropsy at about 8 hands, but her injuries were surgically treatable From them and her clinical condition it can be reasonably assumed that she had lost more than 50 per cent of her blood

Her face was covered with blood, her ears were white, her extremities very cold and the superficial veins greatly constricted She was pulseless and her blood pressure was unmeasurable Extremely restless, she was conscious, the Italian orderlies said that she spoke sensibly about her children and her lost leg, but with difficulty because of great pain Respirations were deep and sighing To the observer she seemed readily revivable by transfusion

★ Because of pronounced venous constriction, difficulty was found in inserting a needle into the veins Though in the head down position, within 10 min she had become unconscious and her respirations were gasping, her head being retracted and her chin thrust out at each inspiration At length a needle was inserted into the left femoral vein and a cannula tied into a forearm vein and, about ½ hr after she was first seen (3 hr after injury), blood was rapidly forced in under pressure at both sites Two bottles of blood and one bottle of plasma were given in 15 min, but she made no improvement and died at the end of the 15 min ★ At necropsy no reason for death was found beyond her injuries Histological examination revealed only a few fat emboli in the lungs and none in the kidneys and brain

Rate of Transfusion

It is clear from both series of patients that, in general, the rise of blood pressure occurred sooner with rapid and later with slow transfusion

There were nine patients in the Home Series, all suffering from much blood loss, with comparable injuries and with blood pressures under 70 In five of these, transfusions of 2–5 bottles of blood or plasma or both were given at a rate of at least one bottle in ¼ hr, and in all the blood pressure rose to normal or almost normal levels within 2 hr In the other four cases, the rate of transfusion of similar amounts was slower, from one bottle in 1¼ hr to one bottle in 2½ hr, in all four the recovery of the blood pressure was delayed till between 3 and 6 hr

With great blood loss, it is of first importance that transfusion should not be delayed and that it should be given at a rapid rate Too slow transfusion not only slows recovery but may result in early death, as the following two examples show

Case H 118, a well developed, healthy man aged 27, was admitted 40 *min* after being injured in a street accident His injuries were very large (about 6 hands), *comprising* a compound, comminuted fracture of the lower end of the left femur with much crushing of the thigh muscles, *four lacerated* wounds of the left knee with severance of the popliteal artery and veins, multiple simple fractures of the lower end of the right femur with some muscular damage, and bruising and abrasions about the posterior superior iliac spine A tourniquet had been applied to the left thigh at the accident but blood continued to ooze

★ Very pale and restless, he was mentally alert and anxious and complained of severe pain His extremities were cold, but there was no nausea or sweating and he was not thirsty The blood pressure was 70/40 (no pulse records) From his wounds and clinical state it can reasonably be assumed that he had lost over 50 per cent of his blood

Another tourniquet was applied, he was put to bed, given morphine ¼ gr and warmed Transfusion was delayed to see whether or not morphine and warmth would suffice for recovery, but he did not improve At 1¾ hr, because of continued bleeding, the tourniquet was reapplied, for persistent pain another ¼ gr morphine was given He vomited undigested food

Transfusion was begun 2 hr after injury and one bottle of plasma was given in ¼ hr and one bottle of blood in ¾ hr By that time, 3 hr after injury, the blood pressure reached 90/55 Transfusion was continued slowly, the second bottle of blood being given in the next 1½ hr and the third over 5½ hr Early during the transfusion of the second bottle, the blood pressure fell to 70/55 and thereafter continued to fall until it became unmeasurable There was no obvious continued bleeding from the left thigh, the right thigh did not swell He complained of thirst after 8 hr and onward After 10 hr he became very weak and died 50 min later

Necropsy revealed no cause for death other than his injuries ★

At the time, this case was regarded as an instance of failure to respond to transfusion and as suggesting that haemorrhage is not the only factor causing circulatory collapse The interpretation in the light of later experience is, however, that the magnitude of the blood loss was not realized and that the patient would have recovered had he been transfused rapidly without delay

In the second case transfusion was slowed and interrupted by the difficulties associated with a transfusion reaction His injuries and clinical state make it seem reasonable to assume that this patient lost at least 60 per cent of his blood Again the interpretation is that he would have recovered had rapid transfusion not been interrupted

★ *Case I* 100, an Italian peasant aged 30, was seen 1½ hr after being injured by a mine He was a fit, strong fellow whose left foot had been blown off, the remaining tissues of his left leg being severely injured There were lacerations of the whole of the back of the right leg from knee to ankle and much tissue was damaged, in all 5–6 hands He was restless, pale, pulseless and cold, and his blood pressure was unmeasurable The superficial forearm veins were very constricted and previous attempts to insert a needle into them for transfusion had failed He seemed conscious enough to understand when told to lie still

A needle was inserted into the right jugular vein and a bottle of serum (500 ml, equivalent to about 9 per cent of his blood volume) was transfused in 10 min He became more restless, had violent rigors and pulled the transfusion needle from the vein A second needle was placed in his left jugular vein and a second bottle of serum was transfused in 13 min His restlessness continued and he had more rigors Even when the head was forcibly restrained it was difficult to keep the needle in the vein At the end of the second bottle, the rigors continuing, his blood pressure was 85/50 and his pulse was palpable at a rate of 128 The respiratory rate was 54 per min After 350 ml of a third bottle of serum, when his blood pressure, measured again

during violent rigors, had risen to 100/50, he once again pulled the needle from the vein. Because of the rigors it was difficult to assess whether he was improved or not, but he was now conscious and mentally clear He was still very cold and thirsty He had been transfused an amount equivalent to about 24 per cent of his blood volume and the observer thought he had some minutes grace in which to cut down on a vein Much difficulty was experienced in cannulating the forearm veins, which were very constricted and tore when a cannula was forced into them, and about ½ hr elapsed before the right saphenous vein was cut down on and easily entered His restlessness had by then ceased, he was pulseless and unconscious Two bottles of blood transfused in 20 min had no effect and at the end of the second bottle he died, 4 hr after injury

At necropsy no cause for death was found beyond his injuries, histological examination revealed many fat emboli in the lungs but none in the brain or kidneys ★

FAILURE OF RESPONSE TO TRANSFUSION

In most cases the initial good response to transfusion was maintained until operation, in some hypotension again developed, in a few the initial response was poor or failed to occur The factors just discussed are sufficient to account for most of these initial or later failures, which occurred mainly in cases with large or very large wounds

Renewed Fall of Blood Pressure

In 15 patients the blood pressure, after rising from hypotensive to normal levels or above as the result of transfusion, fell again, not only when transfusion was stopped but even while it continued

In about half of these, the renewed and usually rapid fall of blood pressure was associated with renewed bleeding In one the haemorrhage was uncontrollable, the femoral vessels having been severed in the groin, and death soon followed In the others haemorrhage was controlled as far as possible, further transfusion was given and the patients were hurried to operation, the blood pressure being restored in some and still low in others For example

Case I 110 a soldier aged 29, was injured by a mine The right foot was mangled and pulped the right thigh grossly lacerated, there was a compound comminuted fracture of the upper part of the left femur with laceration of the soft parts, and the lower half of the left leg and foot was mangled and pulped, elsewhere there were many small cuts and bruises (total tissue damage 7–8 hands) He was given an injection of morphine, probably ¼ gr , soon after injury

Admitted 1½ hr after injury, he was conscious and rational, but air hunger with gasping respirations, restlessness and great distress, pallor, cold extremities, sweating, nausea, thirst, constricted veins, barely palpable rapid pulse (rate not counted) and a blood pressure of 35/? all indicated blood loss to the point of death Blood transfusion was begun at once, and three bottles were given in 24 min During the transfusion an unsuccessful attempt was made to measure the blood volume, there was considerable difficulty in obtaining samples He is thought to have lost 60 per cent of his blood

By the end of the third bottle his colour was returning, respirations were quiet, sweating had ceased and he was becoming drowsy from the morphine given before admission The fourth bottle of blood was given over 23 min and 500 ml serum in 28 min ★He was then much improved, had smoked a cigarette and was intensely thirsty, his blood pressure was 110/50, his pulse rate 132 and his respiration rate 28 Fresh bleeding occurred from the wounds and the blood pressure fell to 85/40, the pulse rate rising to 160 The fifth bottle of blood was at once started and operation began a few minutes later, 1¾ hr after admission, 3¼ hr after injury Before operation

transfusion amounted to the equivalent of 34 per cent of his normal blood volume. He made a good recovery (pp. 73 and 85). ◆

In most of the others the blood pressure fell when transfusion was interrupted or slowed. The blood volume was not measured, but it is probable that the amount of transfusion was insufficient to raise it above the critical level, and that the initial rise of the blood pressure was only partly due to an increase of the blood volume; it seemed partly due to a superimposed transfusion reaction, for when transfusion ceased or slowed and the reaction subsided the blood pressure again fell. It is probable also that continued oozing of blood from the very large wounds contributed in some degree by reducing the blood volume. For example:

Case I 102, a soldier aged 33, was injured by a mine. His left leg was mangled to the knee and the right forearm to the elbow; there were small lacerations of the face, head and neck, and a larger laceration of the right knee. The total tissue damage was 5–6 hands. He was given morphine ½ gr. at once.

◆ Admitted to hospital ¾ hr. after injury, he was still bleeding and seemed to have lost much blood. He was described as 'severely shocked' and vomiting; his blood pressure was 60/30 and his pulse rate 110. Tourniquets were applied and plasma transfusion was begun, though slowly. After two bottles of plasma over 1½ hr. the blood pressure was lower still, 35/? Three bottles of blood and 1500 ml. 2 per cent. soda bicarbonate were given by venous drip over 3½ hr. During this transfusion (accompanied at first by rigors) the blood pressure rose to remain for a time at about 105/70 but again fell to reach 65/? with a pulse rate of 150. At this point, 5½ hr. after injury, operation was begun. He recovered (pp. 77 and 86). ◆

Two of these patients died before operation; *Case I 100* was described on p. 32; in the other case, treatment was abandoned because operation seemed inadvisable.

Case II 120, a man aged 62, sustained in a railway accident very large injuries to his lower limbs (simple fractures of both femora, a compound fracture dislocation of the left knee and a compound fracture of the right ankle, much bruising and tearing of the muscles; total tissue damage 7–8 hands). Much blood was said to have been lost at the accident, and on admission 1½ hr. after injury, his clothes were saturated with blood. ◆ He was given morphine ½ gr. and put to bed with hot water bottles and an electric cradle over him. Fifteen minutes later he was pale, cold and drowsy. His blood pressure was 50/? and his pulse rate 90. One bottle of blood and three bottles of plasma were given in 1 hr.; the blood pressure then was 90/50 and the pulse rate 100. An hour later, at 3½ hr. after injury, the blood pressure had fallen to [illegible] and the pulse rate had risen to 105. Another two bottles of plasma were then given in 1 hr. and the blood pressure rose to 65/40. Surgical opinion then was that double amputation through the thighs was required but was inadvisable on account of the patient's age. Nothing further was done. At 16 hr. his blood pressure was 50/20 and he was still [illegible]. At 20 hr. his blood pressure was 40/? and at 30 hr. he died. Necropsy was not obtained. ◆

Two cases cannot be so explained. In both, transfusion was probably adequate to raise the blood volume above the critical level. In *Case II 115* the renewed hypotension was slight and seemed related to severe pain and passed off when this was relieved by morphine. In *Case I 92* it was profound and was accompanied by extreme cutaneous vasodilatation. This unusual circulatory state was thought to be due to the transfusion of abnormal blood

another patient, not in this series, was transfused on the same day with blood from the same batch and also showed a marked vasodilator reaction

Case H 115, a man aged 43, received very large leg injuries (total tissue damage 7–8 hands) in a railway accident There was a gross compound fracture of the lower end of the right femur with a large wound above the popliteal fossa, at least the lower half of the thigh was crushed and swollen, the muscles forming a jelly-like mass, and the swelling extended into the upper half of the thigh The right foot was crushed and attached only by skin, the lower end of the leg stump was crushed and the leg bones fractured at the junction of lower and middle thirds The left foot had a 3 in wound on the dorsum with crushing of the surrounding tissues *Very much blood was thought to have been lost both externally and into the tissues*

★ *Admitted to hospital 1 hr after injury, he was very pale and cold, the forearm* veins were so constricted that it was difficult to insert a transfusion needle He was *mentally clear and calm, and in great pain Morphine ¼ gr was injected* at once and another ¼ gr 15 min later *He sweated profusely and was thirsty and his tongue was dry* The jugular veins were invisible and did not stand out on finger compression His blood pressure was 80/60 and his pulse rate 100 the radial pulse was very thin An electric cradle was applied and one bottle of serum transfused in 25 min Sweating ceased and the blood pressure rose to 95/68 with rigors A bottle of plasma transfused in 12 min provoked more rigors and the blood pressure rose to 120/80, the pulse rate to 120 He was still pale and looked 'awful', the jugular veins now filled slowly on being obstructed He vomited During the transfusion of a second bottle of plasma over 23 min the rigors ceased the radial pulse became wider and its rate rose at first to 140 and then declined to remain about 120, his extremities became warmer and his face less pale The blood pressure remained between 110 and 120 Two bottles of blood were then transfused over 2 hr During this time the patient experienced spasms of severe pain in his injured leg The blood pressure fell quickly to 90/60, but soon returned to 110/70 when the pain ceased A few minutes later pain returned and continued, the blood pressure fell to 95/60 and the pulse rate remained about 120 Morphine ¼ gr was given, ½ hr later the pain had gone, the patient was *asleep and the blood pressure was once again 120/70 It remained* at that level until operation about 1 hr later At 4 hr after injury, when half the second bottle had been given, venous haemoglobin was 58 per cent *He recovered* (pp 64 and 86) ★

★ *Case I* 92, aged 20, was admitted 6 hr after wounding having lost much blood from a mangled left leg and foot (total tissue damage 4–5 hands) Previously transfused with two bottles of plasma he was pale, cold and pulseless (heart rate 132) and his blood pressure was 50/10 Two bottles of blood were given in ½ hr and the blood pressure rose to 100/20 the pulse rate to 132 A third bottle of blood was then begun but flowed slowly, owing to blocking of the filter, this indicated an unusual amount of clot in the bottles of blood, though none of them showed obvious haemolysis The set was changed and transfusion continued, the blood pressure being 110/70 During the next hour his skin generally became very flushed, the blood pressure *fell to reach 40/? and the pulse rate rose to 168* There was no gross bleeding from the wounds He remained conscious and did not sweat He was sent to operation in this state at 9½ hr after injury *He later died* (p 78) ★

Little or No Response to Transfusion

In addition to *Cases I* 103 and *H* 118, described already (pp 31 and 32), four others also responded poorly to transfusion In all of them inadequate transfusion seems the chief factor responsible In *Case I* 107, who was incompletely *observed*, continuing haemorrhage probably rendered transfusion inadequate and the onset of great restlessness made it difficult to give more at a time when he urgently needed blood

Case I 107, a soldier aged 31 was seen ¾ hr after injury with very large wounds (a large wound of the left thigh laying bare half the thigh muscles with much swelling and a simple fracture of the right femur with much swelling, total tissue damage 6–7 hands) ★ He was very pale and thirsty, but mentally clear, his blood pressure was 50/30, and his pulse rate 92

Over 2 hr he was transfused five bottles of blood (about 40 per cent of his normal blood volume), but continued to bleed considerably from the left thigh, the blood pressure remained about 50 He became pulseless and progressively more drowsy, mentally clouded and restless, and at 3 hr after injury was struggling violently, two orderlies being required to restrain him Struggling interrupted transfusion of the sixth bottle of blood for ¼ hr, operation was begun 3½ hr after injury, the blood pressure being still low ★ He later died (pp 47 and 71)

In two others, also incompletely observed, underestimation of blood loss and inadequate transfusion seem responsible Both patients, however, displayed the unusual feature of marked cyanosis, associated with laboured and deep respirations One died before operation and the other after, in both cases extensive haemorrhages were found in the lungs, in which many fat emboli were revealed

★ *Case H* 112, a man aged 70, received in an air raid gross compound fractures of both legs with much tissue damage (5–6 hands) He had received morphine (? dose) soon after injury, and on admission ½ hr after injury, was given a further ¼ gr and 5 minims of adrenaline (1 1,000) subcutaneously He was placed in the head down position and warmed by an electric cradle, his blood pressure was 70/40 and his pulse rate 100 He remained very restless for an hour and then became quiet Transfusion was delayed until 3½ hr, then two bottles of blood, two of plasma and two of gum saline were given over 3½ hr At 4½ hr after injury he was cyanosed and his respirations were deep and rapid At 8½ hr he was sweating freely, his blood pressure was 78/45 his pulse rate 108, and his respiration rate 34, the electric cradle was only then switched off At 10¼ hr he was still cyanosed and had periods of apnoea his blood pressure was 75/40 and his pulse rate 106 He remained in this state and died 13½ hr after injury

At necropsy, in addition to the injuries, extensive haemorrhages were found in the lungs Histological examination disclosed very many fat emboli in the lungs and many also in the kidneys (brain not examined) ★

Case I 71, a soldier aged about 20 was seen 2 hr after wounding by a high explosive shell He had been given morphine ¼ gr soon after wounding His moderate wounds were a compound fracture of the femur and soft tissue wounds of both legs There was no gross bleeding into the tissues (confirmed at necropsy) Total tissue damage was estimated at 2–3 hands, *evidence of blood loss was lacking His blood pressure was* 60/50 (pulse rate not counted) He was given two bottles of blood and two of plasma with little improvement at 4 hr *after injury the blood pressure was* 70–80/? and his extremities were cold, he was cyanosed and his respirations were laboured and rapid He was sent to operation in this state 5 hr after injury and later died (p 69) ★

Persistent Circulatory Failure

The next case is of considerable interest Throughout our work, both at home and in Italy, we were anxious to see or to hear of instances of persisting circulatory failure, associated with limb wounds and not due to blood loss, which did not respond to transfusion and could not be accounted for by some coincident factor such as infection, coronary thrombosis, or diabetic coma, that is to say, instances of what we heard called "pure shock" We saw none

ourselves and, though from time to time we heard of them, inquiry revealed no convincing case The following is an account of the best documented instance that came to our notice *

★ *Case I* 5, a soldier aged 21, trod on a mine, sustaining small wounds of both legs with very little tissue damage (less than ½ hand) and without injury to any large vessels He was given morphine ¼ gr soon after injury and after a difficult carry over rough country arrived at the Regimental Aid Post 3 hr after injury There he was said to have been in a bad state with a weak and rapid pulse (140) and to have responded poorly to the transfusion of *one* bottle of plasma He was kept 6 hr in the Regimental Aid Post as he was considered unfit to be moved

The observer first saw the patient 11½ hr after injury while he was being carried between Regimental Aid Post and Advanced Dressing Station, another difficult journey which took 3 hr He was very pale and pulseless at the wrist, with a carotid pulse rate of 140 and gasping respirations of 26 per min He lay with his eyes half closed, conscious but unwilling to speak, and answered questions slowly He said he felt cold but had not much pain He vomited three times He arrived at the Advanced Dressing Station at 12 hr in the same state, blood transfusion was started and he was sent on At 13 hr, at the Main Dressing Station, he was still very pale and pulseless, his heart rate was 140 and his blood pressure 70/30, his respirations were shallow and gasping His wounds were not bleeding Blood transfusion was continued, and at 14 hr after injury, during the transfusion of the fourth bottle of blood, his blood pressure was 80/40? By then he was less pale, his extremities were warmer and his respirations shallow but regular At 14¼ hr 2 ml methyl-iso-thio-urea sulphate (? concentration) was injected intravenously, 2 min later his blood pressure was 75/50 The injection was repeated at 14½ hr, and ½ hr later his blood pressure was 80/60 and his face colour was good At 15¾ hr, while the fifth bottle of blood was being transfused slowly, his blood pressure had fallen to 60/50 A third injection of 2 ml methyl-iso thio-urea was given, and 5 min later his blood pressure was 65/60 He was becoming restless and cyanosed, and 16 hr after injury he was given morphine ¼ gr intravenously At 16½ hr he was still very restless and cyanosed, and his respirations were laboured and bubbly, he was unconscious He died 15 min later

At necropsy, 20 min after death, the abdominal organs, brain and heart seemed normal Both pleurae and pericardium contained a small amount (10–20 ml) of serous fluid *An accumulation of serous fluid* between the parietal pleura and the lung substance gave the whole surface of the right lung a yellowish jelly-like appearance A similar accumulation of fluid lay between the lobes of the left lung and extended some way along the bronchial branches Trachea and bronchi contained a large amount of frothy fluid The lungs, brick red on section, *floated in water* No petechiae were seen on pleura, pericardium, heart or brain Histological examination revealed only a moderate number of fat emboli in the lungs but none in the heart, kidney and brain were not examined ★

We do not know how to interpret this case The clinical picture is that of gross blood loss and failure of response to delayed transfusion The small wounds, however, seem to exclude significant haemorrhage We did not see the patient during life, and after death could examine only the heart and lungs after they had been removed from the body

* We are indebted to Capt T B McMurray R A M C for the details of this case

Course During Operation

INTRODUCTION

We have followed these patients through the period immediately succeeding their first trauma, and now consider what happened when they were subjected to a second, namely, operation Operation may justly be regarded in this light, more tissue is damaged, more blood is lost and the injured limbs are subjected to manipulation which, for the reduction of fractures, is often forcible It is not surprising, therefore, that the circulatory changes during operation are very similar to those already described

We first deal briefly with the time of operation after injury, the duration of operation and the anaesthetic agents used We then describe the circulatory disturbances occurring during operation, indicating the factors responsible for them Finally we give evidence of the prime importance of the level of the blood volume during operation by showing that the various factors acting on the circulation are more liable to provoke circulatory collapse in patients whose blood volumes are near the critical level than in others

Time of Operation after Injury

This is shown in Table 10 It ranged from 1¾ to 38 hr in the Home Series (average 6½ hr) and from 1 to 54 hr, in the Italian Series (average 11 hr)

The longer interval between injury and operation in the Italian Series was due to later admission to hospital Table 11 shows the interval between

TABLE 10

Interval between injury and operation patients with limb injuries

Time (hr)	0–2	2 01 –4	4 01 –6	6 01 –12	12 01 –18	18 01 –24	24 01 –36	Over 36
Italian Series (93 cases)	3	6	18	43	10	6	4	3
Home Series (108 cases)	10	40	23	21	9	2	1	2

Cases are omitted if the time interval is not known

TABLE 11

Interval between admission to hospital and operation patients with limb injuries

Time (hr)	0–2	2 01 –4	4 01 –6	6 01 –12	12 01 –18	18 01 –24	24 01 –36	Over 36
Italian Series (86 cases)	27	39	13	7	—	—	—	—
Home Series (104 cases)	29	41	13	12	6	—	2	1

Cases are omitted if the time interval is not known.

admission to hospital and operation to be on the whole shorter for the Italian Series, 93 per cent of these cases were operated on within 6 hr of admission compared with 80 per cent in the Home Series

It is noteworthy that in the Italian Series operation on patients with large and very large wounds was begun within 4 hr of admission in all but two cases and in these two within 6 hr, while in a third of these patients in the Home Series it was delayed beyond 6 hr (7½–17½ hr)

In the Home Series delay resulted in high mortality

There are 16 patients in the Home Series comparable in age and other respects and all with extensive injuries to both legs Half were operated on between 1 hr and 4½ hr after the injuries and three of them died In the other half operation was delayed till between 6½ hr and 18 hr and only one survived

A number of factors contributed to this increased mortality in the second group Transfusion on the whole was begun later and less was given than to the early operation group, and the longer interval between injury and operation gave more opportunity for the development of infection

In the Italian Series, on the other hand, delay in operation is not associated with much increased mortality

There were 14 patients with very large injuries to both legs Half were operated on within 6 hr and two died On the other half operation was delayed till between 7 hr and 24 hr after injury, and three died

The Italian Series were earlier and better transfused than the Home, and treatment with sulphonamides was usually begun soon after wounding

Duration of Operation

The duration of operation, shown in Table 12, is counted from the beginning of the anaesthetic to the end of bandaging This gives a better

TABLE 12

Duration of operation patients with limb injuries

Time (hr)	0–0 5	0 5–1	1 01–1 5	1 5–2	2 01–3	3 01–4
Italian Series (84 cases)	24	36	15	5	3	1
Home Series (107 cases)	34	57	9	5	2	—

Cases are omitted if the duration of operation is not known

measure of the period during which the patient is subjected to factors disturbing the circulation than does the surgeon's operating time For it will be shown that the anaesthetic and the manipulation of the limbs may affect the circulation not only while the surgeon is operating, but also during the preparation of the limbs beforehand and the application of the plasters and dressings afterwards In both series, operation lasted on the average just under 1 hr, although much longer in a few patients

Anaesthetic Agents

In the Home Series a mixture of nitrous oxide, ether and oxygen was used for about half the patients, ether for about a quarter and oxygen and nitrous oxide for the remaining quarter In most cases these agents were used for both induction and maintenance, in some anaesthesia was induced by "Pentothal", ethyl chloride, etc Various other agents and combinations, including local and spinal anaesthetics, were used for a few

In Italy "Pentothal" (often with oxygen by mask) and ether and oxygen (mostly preceded by ethyl chloride or "Pentothal") were each used for about one third of the cases In the remaining third the nitrous oxide, ether and oxygen mixture, cyclopropane, chloroform and other agents were employed

The volatile anaesthetics were administered sometimes by the open method but usually by the Oxford vaporizer or by Boyle's or Heidbrink's apparatus

CIRCULATORY CHANGES

We will consider the patients in two groups, those in whom the blood pressure was 100 or over at the beginning of operation, who constitute the great majority of both series, and those coming to operation with a low blood pressure

Patients Coming to Operation with Blood Pressure 100 or Over

Vasoconstriction, if initially present, had more or less passed off, most were warm and their facial colour was good or had improved since admission, some were still pale though warm, in some the extremities remained cold In the large majority of those transfused the pulse rate was fast and in a considerable proportion some degree of pallor and coldness persisted We have seen reason to believe that in both series the pre-operative transfusion had been sufficient to raise the blood volume to about the critical level or above, though insufficient to restore it to normal

Circulatory changes were very common during operation in both series of cases Changes of blood pressure, both increase and decrease, were often accompanied by constriction or dilatation of the cutaneous vessels, and by increase or decrease of the pulse rate In our description emphasis is laid on the blood pressure because, during operation as well as before, it provides the best guide to the state of the patient

These circulatory changes are more complex in origin than those of the pre-operation period, for during operation new factors are added to those already at work Up to the time of operation the circulatory state is influenced by the amount of blood loss, by the amount and pharmacological properties of the transfusion, by the medication, by nervous stimuli arising from the injuries and from the patient's emotional state, and by the age of the patient During operation it is influenced also by the pharmacological properties of the different anaesthetic agents used, by the difficulties associated with their administration, by further transfusions and by the surgical procedures In the surgical procedures three factors are to be distinguished, (i) further haemorrhage, (ii) fresh tissue damage by the surgeon, and (iii) manipulation of the injured parts Transfusions at operation not only increase the blood

volume but also exert pharmacological effects, though rigors are rarely seen as a result of a transfusion during the actual administration of the anaesthetic The warming or cooling of the patient on the operating table also exerts an effect In Italy especially, the scantily clad patients were often exposed for periods of half an hour or more to the air of the operating room or tent, which was not always well heated, and were therefore liable to a considerable heat loss, particularly so if anaesthetic agents increased blood flow through the skin

The parts played by some of these factors can only be indicated roughly Further analysis under more simplified conditions is required to define the precise effects of a particular factor under given conditions

Rise of blood pressure A rise of blood pressure was transient or long-lasting according to the factor responsible and was associated with a slowed, increased or unchanged pulse rate and with constricted or dilated cutaneous vessels

A transient rise of blood pressure was seen in a few cases when the patient was taken to the operating theatre and placed on the table, before anaesthesia was induced, and was probably emotional in origin For example

In *Case I* 47, with compound fractures of femur and tibia (moderate wound), the blood pressure rose from its previous level of 125/80 to 200/150 immediately before the injection of 'Pentothal' He fell asleep after 5 ml had been injected in 3 min Four minutes later his blood pressure was 145/50 and 4 min later still it was 130/50, about which level it remained during a ½ hr operation

A transient rise of blood pressure was also provoked by stimuli which would normally cause pain, in unconscious as well as conscious subjects

Case H 28, a fit man aged 28, accidentally sustained a compound fracture of the right radius 3 in above the wrist, together with a dorsal dislocation of the ulna, 2 in of bone protruded, the wound was small and little blood had been lost

Seen about ½ hr after injury, he was suffering severe pain His colour was good, his extremities warm, his blood pressure 165/90 and his pulse rate 78 He was given *morphine ¼ gr and the pain soon eased*, the blood pressure fell to 145/80 and remained about that level till operation 2¼ hr after injury

At the beginning of the injection of 'Planocaine' to induce a brachial block, the blood pressure rose to 175/80, but it soon sank to 160/78 and remained about that level *till injection was ended 14 min later* Débridement of the wound was begun 4 min later, the blood pressure rose to 180/76 and remained thereabout for 10 min, when general anaesthesia was induced by nitrous oxide, ether and oxygen The blood pressure quickly fell to remain about 125/55, while the wound was excised Then traction was applied manually to reduce the fracture The blood pressure first rose to 140/55, then quickly fell to 95/55, while the pulse became very weak *(rate not counted)* Within 4 min it had returned to 120/50 When the anaesthetic was withdrawn, ¼ hr later the blood pressure was 125/55, and it remained about that level thereafter

Case H 21 a man aged 54 accidentally sustained a crushing injury of his right foot (small wound)

Seen ¾ hr later, he was pale shivering a little and in much pain, his blood pressure was 135/65 and his pulse rate 52 The dressings on the foot were soaked with blood He was warmed under an electric cradle and given morphine ¼ gr Half an hour later his blood pressure was 135/70 and his pulse rate 60 He was then given atropine sulphate $\frac{1}{50}$ gr and sent to operation ½ hr later, with a blood pressure of 140/70 and a pulse rate of 90

Anaesthesia was induced with chloroform ether mixture and continued with ether and oxygen A tourniquet was applied to the leg, and for this the foot was much moved His blood pressure, which had previously been 140/80, fell to 115/80 for about 3 min, recovering to 130/70 Two minutes later, when an encircling incision was made round the leg, the blood pressure again fell to 115/70, recovering to 125/80 3 min later During the sawing through the bones of the leg the blood pressure rose to 140/90, and to 150/90 while the vessels were being tied, 2 min later it was 140/90 and the pulse rate 120, and 10 min later still 115/75 and 116 The operation finished 5 min later, the blood pressure remaining unchanged

The administration of nitrous oxide was often associated with a prolonged rise of blood pressure, due probably to asphyxia In some cases, but not all, the blood pressure, though fluctuating, remained raised during operation (e g a rise from 114/62 to between 140/60 and 190/106) and returned to about the pre-operative level after the anaesthetic was withdrawn

The rise of the blood pressure associated with respiratory obstruction during the administration of the anaesthetic is referred to later

Fall of blood pressure A fall of the blood pressure below 100 was common in both series of cases According to the character of the fall and the associated phenomena, several different vascular reactions can be recognized and associated with particular stimuli

1 A rapid and transient fall of blood pressure accompanied by an increase of pulse rate may follow the rapid injection of "Evipan" or "Pentothal" For example

In *Case H* 43, with a moderate wound of the calf, no great blood loss, and a circulatory state that had remained normal without transfusion, blood pressure fell steeply from 105/60 to 70/50 and the pulse rate became temporarily very rapid during the injection of 6 ml of Evipan Trilene' and nitrous oxide were then given and the operation proceeded In 20 min the blood pressure had returned to 100/70 and the pulse rate to 72, the skin remaining pink and warm

In *Case I* 2, with minor flesh wounds, negligible blood loss and a normal blood volume, the injection of 1 3 g 'Pentothal over 8 min resulted in a rapid fall in blood pressure from 120/80 to 90/60, the pulse rate rising from 90 to 130 The blood pressure was restored to normal within 10 min, while the pulse rate remained fast

2 A rapid and transient fall of blood pressure accompanied by a decrease of the pulse rate and sometimes by signs of vasoconstriction, such as narrowing of the radial pulse, facial pallor and cooling of the extremities, may result from manipulation of the injured parts This reflex depression of the vasovagal type has already been noted as occurring in the pre-operative stage It may also occur at operation, during the movement of the fractured limb in preparation for surgery, extension for the reduction of fractures, application and release of a tourniquet or application of forceps to pick up a bleeding point The nature of the effective stimulus requires further definition under more controlled conditions than we have attained, but it seems usually to be a manipulation likely to cause pain in the conscious subject It was seen in several patients of the Home Series in whom a local anaesthetic was used and in patients of both series during general anaesthesia For example

Case H 8 was lying on the operating table while his head was being shaved preparatory to suturing a 1½ in wound of his scalp, his only injury, under local anaesthetic

His blood pressure was 110/70 and his pulse rate 100 He complained of pain and became pale, nauseated, restless and then quiet Within 5 min the blood pressure had fallen to 60/? and the pulse rate to 88, the pulse becoming thin and difficult to feel He wanted to open his bowels and pass water He remained in this state for 10 min , but quickly recovered when the head of the table was lowered

In another case under "Evipan and nitrous oxide, the systolic blood pressure fell during the manipulation of the leg from 150 to 45, 5 min later it was 80 and then gradually rose to remain between 90 and 100, the pulse rising from 105 to 140, coldness and pallor persisted for some time

These transient falls of blood pressure resulting from manipulation are often dismissed as unimportant In the examples quoted this estimate is true enough, but the factors causing them can in other circumstances provoke more profound, enduring and dangerous falls They are therefore important as revealing those factors which depress blood pressure, and they give warning to surgeon and anaesthetist that care is required in the further management of the case Disregard of the warning sometimes results in death For example

Case H 113 was admitted 1¼ hr after sustaining a very large injury comprising gross, compound, comminuted fractures of both legs and a non penetrating wound of the loin with much tissue damage and blood loss (total damage about 5 hands) He had received morphine ½ gr and had been warmed, and tourniquets had been applied to both legs On admission he was given another ¼ gr morphine and warming was continued with an electric blanket At 2 hr after injury he was fairly clear mentally, still in pain, very thirsty and very pale, and his extremities were cold, he sweated profusely, his blood pressure was 55/40 and his pulse impalpable, heart rate 120 and respiration rate 24 ★From his injuries and clinical state his blood volume was thought to be probably not more than about 50 per cent normal ★

There were delays and difficulties in starting transfusion An attempt to transfuse reconstituted serum resulted in only 40 ml entering the vein Finally, beginning at 3¾ hr , when his blood pressure was unmeasurable, two and a half bottles of plasma were given in ½ hr His blood pressure rose to 115/75 and the radial pulse became palpable, its rate 110 Transfusion of the remaining half and of a fourth bottle of plasma was continued slowly, the blood pressure was maintained

Operation was delayed till 6¼ hr after injury, by which time he had been transfused three and a half bottles of plasma and 40 ml serum, an amount equivalent probably to no more than 20 per cent of his blood volume While awaiting operation he was given another ¼ gr morphine, making 1 gr in all since injury, and $\frac{1}{300}$ gr hyoscine He was anaesthetized with nitrous oxide, ether and oxygen, plasma transfusion continuing slowly ★An hour was spent cleaning and excising the wounds, at the end of this time his blood pressure, initially 115/80, had fallen to 95/45 and his pulse rate had risen from 96 to 120 When one leg was manipulated prior to the application of the plaster, his blood pressure fell steeply to 65/40 and pulse rate to 88 Transfusion was speeded under pressure but without effect on the blood pressure Nevertheless the operation was continued on the other leg, and when this was extended the patient died Five and a half bottles of plasma had been given by then ★

At necropsy, nothing was found to account for his death beyond his injuries, the blood was noted to be very watery

3 A third vascular reaction is one in which the fall of the blood pressure is gradual and enduring and is accompanied by signs of vasodilatation (warm and flushed skin, relaxed and full veins and wide radial pulse), and sometimes by sweating It appears to be due mainly to the anaesthetic agents, ether, cyclo-

propane and chloroform, though it is difficult to exclude the simultaneous participation of other factors and especially a blood volume near the critical level The pulse rate is variously affected according to the anaesthetic agent used, it is increased by ether, a little slowed by cyclopropane and markedly slowed by chloroform The reaction soon passes off when the anaesthetic is withdrawn

In *Case H* 24 8 oz of ether were given by the Oxford vaporizer over 1 hr during an operation on a compound fracture dislocation of an ankle The patient s circulatory state had remained normal while he was observed before operation (from $2\frac{1}{4}$ hr to 6 hr after injury) and he was not transfused Blood loss was thought initially to have been less than 20 per cent of his blood volume He continued to bleed slowly until operation, his dressings becoming soaked with blood ★ The anaesthesia was smooth, manipulation gentle, and blood loss slight The blood pressure fell gradually from 120/70 to 70/45 and the pulse rate rose from 90 to 120 The patient initially warm and of good colour, became hot, flushed and sweating, and his arm veins became prominent Ten minutes after the ether was stopped his blood pressure was 90/60, and 20 min later 105/60, the pulse rate was then 100 and the patient less flushed and no longer sweating ★

It is to be noted that, though both ether and cyclopropane appear regularly to produce a marked cutaneous vasodilatation, the blood pressure does not always fall It is more likely to fall if the blood volume is near the critical level than if it is normal In the few cases in which it was used chloroform caused a marked fall of the blood pressure and cutaneous vasodilatation together with great slowing of the pulse rate "Pentothal", if given rapidly, lowered the blood pressure and increased the pulse rate, it seemed to have little effect on the cutaneous vessels

4 A fourth reaction to be recognized is a more or less rapid and enduring fall of the blood pressure accompanied by an increase of the pulse rate and cutaneous vasoconstriction, sweating is sometimes added and occasionally vomiting In most instances it is associated with renewed bleeding (*Case H* 61, p 70), but in some with manipulation of the injured parts, as the following example shows

Case H 67, a man aged 30, was seen $2\frac{3}{4}$ hr after a railway accident in which he suffered a compound fracture of the lower part of his right leg with tearing and crushing of all the calf muscles (tissue damage 3–4 hands) He was judged to have lost about 20 per cent of his blood

He had little pain and was mentally clear, quiet, not anxious and comfortably warm, his face was a fair colour, his blood pressure was 130/80 his pulse rate 112 and his radial pulse thin Morphine $\frac{1}{4}$ gr was given Blood continued to ooze from his wound At $3\frac{3}{4}$ hr after his injury his blood pressure was 105/80 and his pulse rate 128 (40 min previously he had received atropine $\frac{1}{100}$ gr) No transfusion was given, but it was thought he would require it during operation

Operation (amputation above the knee) started 4 hr after injury and lasted $1\frac{1}{4}$ hr, anaesthesia being induced and maintained by ether (Oxford vaporizer) without difficulty Very little blood was lost

★ During the preparation the leg was moved considerably, the blood pressure fell steeply from 110/60 to 50/40, the pulse rate was 140 and the radial pulse very thin, the hands were cool and sweating Blood transfusion was started 5 min later and amputation begun The transfused blood would not run in freely at first but its rate increased gradually, probably with the passing off of venous constriction Ten

minutes later, at the end of the first bottle, the blood pressure was 85/60 and the pulse rate 130 Sawing through the femur did not alter the blood pressure or the pulse rate, which at the end of amputation were 90/55 and 112 respectively ★ Tilting the table head down raised the blood pressure to 100/60 Transfusion was continued, two more bottles being given over 1 hr During this period the blood pressure rose and the pulse rate declined further, the radial pulse became wider and the hands warmer, sweating ceased When the anaesthetic was withdrawn and the table returned to the horizontal at the end of operation the blood pressure was 110/80 and the pulse rate 96 Circulation was thereafter maintained

Not all falls of blood pressure witnessed at operation in these cases can be fitted into any one of the foregoing types, nor is it always possible to point to any one factor as mainly responsible for the depressor reaction Nevertheless there is abundant evidence that the anaesthetic agent, renewed haemorrhage and manipulation can each act separately or in combination to lower blood pressure There remains for consideration another factor that may profoundly influence circulation, namely disturbance of respiration

Changes of blood pressure with respiratory disturbance Some attention was paid to respiratory disturbances in the Home Series, but more in the Italian, and what follows is derived chiefly from the experience of the latter Changes in rate and depth of respiration were common, especially with ether and cyclopropane anaesthesia Periods of apnoea were common with cyclopropane and in a number of cases artificial respiration was required for considerable periods

The respiratory disturbances seemed due mainly to difficulties in the administration of the anaesthetic The most common difficulty was a varying degree of obstruction to the air passages which, if of sufficient magnitude, disturbed the aeration of the lungs, resulting in carbon dioxide accumulation and lack of oxygen, and loaded the acts of expiration or inspiration or both, depending on the type of obstruction In the cases observed obstruction arose in a variety of ways, not only during induction but also later, for example, from a narrow airway or endotracheal tube, from tight valves on the anaesthetic machine and from vomiting A deficiency of oxygen or an excess of carbon dioxide alters not only the rate and depth of respiration but also the pulse rate, the blood pressure and the calibre of the cutaneous vessels Further, the movements of the thorax influence the filling of the heart

It has not been possible in the circumstances to analyse the varying circulatory effects of combinations of too little oxygen, excess carbon dioxide, increased respiratory load, varying anaesthetic agents, varying operative procedures and varying amounts of blood loss, this more careful definition awaits further work But two forms of circulatory reaction were frequently seen during the administration of the anaesthetic The first was an exaggeration of the normal respiratory variations of the blood pressure, which falls during inspiration and rises during expiration, in extreme instances the variation in systolic pressure reached 50 mm Hg or more The second was a rise of blood pressure associated with obstruction to respiration, which might or might not be associated with an increased pulse rate or cyanosis and was seen during "Pentothal", ether and cyclopropane anaesthesia It might be combined with

exaggerated respiratory variation On removal of the obstruction the blood pressure fell to its original level or lower Probably other types of circulatory reaction occurred, but these could not be disentangled from the clinical pictures with their multiple causations

In the Italian cases some degree of respiratory obstruction was very commonly present, most often with ether and least often with "Pentothal", which probably accounts for the fall of blood pressure which occurred in a number of cases when the anaesthetic mask was removed at the end of operation Often at that time dressings or plasters were being applied, necessitating considerable movement of the patient, so that the origin of the fall is not always certain In a few cases the mask was reapplied and the blood pressure again rose, only to fall again on its removal

On removing an obstruction the blood pressure fell very rapidly, usually to normal levels or a little below, and either remained there for some time or soon rose again slightly In certain cases, however, it fell to dangerously low levels The probable explanation is that during operation the patient is subjected not only to a pressor stimulus from the administration of the anaesthetic, but also to a depressor, arising for example from renewed blood loss The pressor factor either just balances the depressor, so that the blood pressure remains about normal levels, or predominates and produces a rise in blood pressure The removal of the pressor factor allows the depressor to display itself in a fall of the blood pressure

Case I 79, a prisoner of war aged 21, was seen 6½ hr after a mine had disarticulated his right foot and damaged the tissues of the lower half of the right leg (total tissue damage about 3 hands) He had received morphine ¼ gr soon after the injury but still suffered considerable pain His wounds were infected He was pale, warm, mentally alert and anxious His blood pressure was 140/80, his pulse rate 106 He was given another ¼ gr morphine During the 3 hr between admission and operation the blood pressure remained about this level, the pulse rate increased to 120 He remained pale and his extremities became cool His blood volume, measured 8 hr after injury, was 70 per cent of his predicted normal, blood pressure was then 130/80 and pulse rate 106 Just before operation $\frac{1}{100}$ gr atropine, given intravenously, increased his pulse rate from 120 to 140 No transfusion was given

Operation was begun 9½ hr after injury and lasted ¾ hr Anaesthesia, induced by "Pentothal" (0 4 g), was maintained by Trilene (5 ml) with oxygen through Boyle s apparatus Carbon dioxide accumulated in the air of the apparatus and the patient developed very deep respirations, varying in rate between 30 and 40 The hyperpnoea and hyperventilation made his pulse rate rise to between 160 and 180 and his blood pressure show a marked respiratory variation of 30 mm Hg or more The leg was amputated below the knee with a loss of about 5 per cent of his blood volume ★The blood pressure was maintained between about 120 and 160 mm Hg, the two values being at the beginning of expiration and inspiration respectively He became warm and sweated profusely On removing the mask, respirations soon quietened and sweating ceased, within 10 min the blood pressure fell to 35/ ? and the radial pulse became impalpable, the temporal pulse remained palpable, its rate being 176 He was removed to the ward in this state ★

One hour after operation he was still under the anaesthetic He was warm, with a fairly good face colour, and not sweating, his blood pressure was 70/45, his pulse rate was 124 and his respirations were 16 His blood volume was measured and found to be 64 per cent of the predicted normal He recovered (p 66)

This seems to be an instance in which the blood pressure was maintained by the respiratory pump with a blood volume under the critical level In a similar case (*Case I* 104, p 55), where administration of the anaesthetic again resulted in hyperpnoea and hypertension, but where the blood volume was normal during operation removal of the mask brought the blood pressure down from the hypertensive level, but not to below 100

These are extreme examples, but it is clear from our observations that the administration of an anaesthetic not infrequently provides a pressor stimulus, which may overcome any depressor factor, but when the pressor stimulus is removed at the end of operation, a time when often the surgeon has left the completion of the plaster and dressings to his assistants and the anaesthetist is busy with the preparation of the next case, the patient may fall unnoticed into a dangerous state of circulatory collapse

Patients Coming to Operation with Low Blood Pressure

These 23 patients had all lost much blood and had blood volumes known or judged to be below the critical level, most had large or very large wounds, most had been transfused before operation, almost all were pale and cold and had a fast pulse rate

These cases were recognized to be seriously ill, so operation was kept as short as possible (in a number two surgeons operated) and transfusion was given to the majority In the circumstances, it was not often possible to follow in detail the circulatory changes taking place or to relate these to the various causative factors Nevertheless, it is clear that (i) the general result of operation in these cases was a further lowering of the blood pressure, often to dangerously low levels, vasoconstriction and a fast pulse rate persisting or increasing, (ii) these circulatory changes were again the resultant of the pressor and depressor factors discussed above

Case I 107, who had very large thigh wounds and continued bleeding, was inadequately transfused and had persistent low blood pressure (p 36) He came to operation 3½ hr after injury Anaesthesia, induced by ethyl chloride, was maintained by ether (Oxford vaporizer) Transfusion was restarted During the 20 min operation, the left leg was amputated through the upper thigh and about 300 ml blood was lost

★While the leg was being manipulated the blood pressure, which had been 45/?, became unmeasurable, and the pulse slowed from 120 to 80 Transfusion had been going badly, but was then given rapidly, he received the sixth, seventh and eighth bottles of blood over ½ hr His blood pressure remained unmeasurable and his pulse rate rose to 160, his extremities were cold and his veins greatly constricted He died soon after the operation (p 71) ★

Case I 108*, a soldier aged 23, trod on a mine, receiving very large leg injuries Both feet were partially amputated and both legs mangled and pulped to the knees, there were several small penetrating wounds of the right arm Morphine ¼ gr was given soon after injury

Seen at 1¾ hr after injury, he was drowsy, mentally confused, cold and pulseless, his face, lips and ears were very pale Blood transfusion was started at once and four bottles were given over 24 min, his blood pressure was then 80/30 and his pulse rate about 132 Free bleeding occurred from both legs, tourniquets were applied and transfusion continued By the end of the eighth bottle of blood, at 2¼ hr after injury,

* We are indebted to Capt R P Maybin, R A M C for details of this case

his blood pressure during slight shivering was 110/80 and his pulse rate 120, colour *had returned to lips and ears* He was still confused, but became mentally clear during the transfusion of the ninth bottle of blood over the next ½ hr, his blood pressure fell, however, to remain about 95/60, and after the administration of atropine $\frac{1}{100}$ gr his pulse rate rose to 160

Operation, *begun at 3¾ hr* after injury, lasted ¾ hr under anaesthesia induced by 0 2 g Pentothal and maintained by ether and oxygen (*Boyle s apparatus*) ★ *Both* legs were amputated above the knees and the stumps put in plaster Transfusion was *continued with the tenth* bottle of blood and 400 ml double strength serum His blood pressure initially 95/60, fell during *amputation to 60/? but soon recovered to* remain about 85/60, his pulse rate remained about 160 throughout He recovered (pp 74, 83) ★

Case H 119, a man aged 57, sustained in an accident very large injuries (left leg severed above knee, right femur fractured in mid shaft and just above the condyles, much bruising and tearing of soft parts) *A tourniquet was soon applied to the left* thigh The patient was admitted to hospital 20 min after the accident and was given morphine ¼ gr At ¾ hr after injury he was pale, in pain, nauseated, sweating freely and moaning, *his hands were cool, his blood pressure was 80/60 and his pulse rate 114*

★His clothes were cut off and operation began 1 hr after injury under open ether The left leg was amputated at mid thigh and a Thomas s splint was applied to the right Very little blood was lost Probably because of some respiratory difficulty, the systolic blood pressure, which had been raised during induction, fell again to fluctuate between 80 and 90, the pulse rate remained between 120 and 130 Manipulation did not appear to provoke any greater fall of blood pressure When the anaesthetic was withdrawn at the end of the ¾ hr *operation the blood pressure fell quickly to 60/40* He subsequently died (p 74) ★

Though these patients remained seriously ill during operation, experience of the Home Series shows that the circulatory state was better on the whole in those transfused during operation than in the others Thus half of the fourteen patients of the Home Series in this group were not transfused during operation, in all of them the blood pressure fell considerably, to 50 or below in two, one of whom died In four of the transfused patients the blood pressure remained about its initial level or fell lower, but in all the rest it was raised, and in one it was restored to normal by the end of operation As an example, two cases may be compared, one of whom was transfused at operation while the other was not, the one transfused had the larger injuries

Case H 104, a man about 48, received large wounds of the legs in an air raid (traumatic amputation of the right leg below the knee and of the left below the ankle) Morphine ¼ gr was given soon after Bleeding continued when he was *admitted to hospital 1 hr after injury* Tourniquets were applied to both limbs, the bed foot was raised and he was warmed by an electric cradle At 1½ hr after injury morphine ¼ gr and adrenaline 10 minims ($\frac{1}{1000}$ solution) were administered subcutaneously ★*The* transfusion was begun 2 hr after injury and three bottles of blood and one of plasma, given over 2 hr, raised his originally low blood pressure to 95 50 His pulse rate was 160 He was pale, nauseated and very thirsty An hour later his blood pressure had fallen to 65/35 and his pulse rate to *140 Three bottles* of blood were given over 5 hr and raised his blood pressure to 115/75 (pulse rate 136) His blood pressure again declined to 95/60, he was given atropine $\frac{1}{100}$ gr, but no further transfusion, and sent to operation

Operation under *nitrous oxide*, ether and oxygen anaesthesia began 12½ hr after injury, the patient being kept in the head down position His blood pressure was not measured, but to judge from the pulse it fell very low *Amputation of both legs above*

the knees occupied ½ hr As the flaps were being stitched, the patient died ★Necropsy was not obtained

Case H 114, a woman aged 32, received large wounds in an air raid (grossly compound fracture of femur, compound fracture of radius and ulna, much bruising and tearing of the soft parts) ★Admitted 1 hr after injury, she seemed very ill, she was given morphine ¼ gr, warmed and given three bottles of plasma over 2¾ hr, suffering rigors during the transfusion At 4¼ hr after injury, during a rigor, her blood pressure was 120/45 and her pulse rate 140, she was conscious and very pale and her extremities were cold At 5 hr after the injury, when her rigors had ceased, her blood pressure was 110/50 and her pulse rate 148 A bottle of blood was transfused slowly, her blood pressure fell further to remain about 95/45 and her pulse rate increased to between 160 and 180, she remained very pale A second bottle of blood was started and operation began at 8 hr after injury

At operation, lasting 1 hr under nitrous oxide, ether and oxygen anaesthesia, the left leg was amputated through the upper thigh and the forearm treated conservatively The second and part of a third bottle of blood were transfused At the end of operation her face colour was good and she sweated profusely, her blood pressure was 105/50, her pulse rate 160 She recovered (p 63) ★

IMPORTANCE OF THE LEVEL OF BLOOD VOLUME

In both series of patients, the more profound and enduring falls of blood pressure at operation occurred in those who had already lost much blood Their blood volumes at the beginning of operation were in most cases not much above the critical level, and in some below it Moreover, they had extensive wounds which were apt to bleed afresh when treated surgically, and when blood volume is near the critical level a relatively small haemorrhage will reduce it below this level and thus precipitate a fall of the blood pressure Even those suffering very little haemorrhage at operation were unable to maintain their circulation, so it seems that the other depressor factors acting on the circulation during operation are, like haemorrhage, more liable to cause severe depressions in patients with a blood volume near the critical level than in others Strong evidence of the prime importance of the level of the blood volume during operation is derived from a closer analysis of the Italian Series, which provides sufficient cases with measured blood volumes and adequate data on the operative course and anaesthesia to allow the importance of the various factors in causing circulatory disturbance to be assessed

Patients Anaesthetized with "Pentothal" Only

These 19 patients received similar dosages of "Pentothal", so far as can be judged they experienced similar depths of anaesthesia, and in few of them did the administration of the anaesthetic produce any difficulty, in particular any respiratory obstruction, so that anaesthetic differences cannot be considered as the main cause of circulatory differences The patients were all young men with varying amounts of tissue damage and haemorrhage, and experienced varying operative procedures In most of them the external blood loss during operation was measured, the amounts and rates of transfusion are known, the blood was sampled fairly frequently, and one or two blood volume estimations were made near the time of operation, so that the blood volume

during operation can be calculated with fair accuracy and the effects of haemorrhage assessed If the patients are arranged in order of the percentage of their predicted normal blood volume remaining at the beginning of operation, it is clear that falls of blood pressure occur mainly in those with the lower blood volumes

Thus of seven cases with blood volumes of 90 per cent or more, only two showed transient falls of blood pressure, in one case to 90 and in the other to 80

Of six cases with blood volumes between 75 and 80 per cent, again only two showed transient falls

Of five with blood volumes of the order of 70 per cent of the predicted normal, only one failed to show a sustained fall of blood pressure

The evidence that the blood volume during operation is of the first importance can be further strengthened by comparing cases closely similar in their injuries, dosage of "Pentothal" and surgical procedures, but differing in the percentage normality of their blood volumes at the beginning of operation

Thus, there are three cases with closely similar injuries (traumatic amputation of a foot), anaesthetics and surgical procedures

One (*Case I* 41) had bled very little and his blood volume at operation was normal Although he had the largest dose of Pentothal he showed no fall of his blood pressure but rather a slight rise during operation His blood pressure returned to normal after operation

The other two had bled much more One (*Case I* 44) had a blood volume of 70 per cent (rather more than maintained by transfusion at operation) and the other (*Case I* 51) a blood volume of about 75 per cent (rather less than maintained by transfusion) Both showed sustained falls of blood pressure, in both the blood pressures returned to normal with the continuation of transfusion after the end of operation

It appears therefore that the critical level of blood volume for a sustained fall of blood pressure under "Pentothal" anaesthesia is in the region of 70 per cent of the normal

The periods of low blood pressure in this group of patients are usually associated with fresh haemorrhage or manipulation or both Most of the patients suffered considerable manipulation during the removal of dressings and splints, the cleaning of the limbs, the application and removal of tourniquets, the supporting of fractured limbs, the cutting of soft tissues and sawing of bones There was, therefore, much opportunity for originating reflexes Certain comparable cases illustrate these points

There were two cases with compound fractures of the femur near the knee joint, who lost initially 40–45 per cent of their blood, both were anaesthetized with 1 3 g Pentothal , their operations were approximately of the same duration and both underwent amputation of the thigh Both experienced considerable manipulation of the injured limbs and both bled less than 500 ml at operation

*In one of them (*Case I* 57,) the blood volume at the beginning of operation was about 75 per cent and was maintained at this level by slow transfusion The blood pressure fell steadily from 120 to 80 over 25 min , the fall being associated with the manipulation, preparation and amputation, and perhaps also with the injection of Pentothal Twice during the fall of the blood pressure the pulse rate slowed temporarily from its average level of about 130, to 70 and 80 respectively, the slowing being apparently related to manipulation of the damaged limb (vasovagal type of response) The face was pale, the hands were cold and the veins constricted before operation (transfusion

reaction) and remained so till after operation ★ The blood pressure was restored to normal levels 20 min after amputation of the leg by lowering the head of the table and by further transfusion

★In the other (*Case I* 73) the blood volume at the start of operation was about 80 per cent and was increased by transfusion during operation to about 85 per cent Although the patient was subjected to much the same stresses during operation, his systolic blood pressure remained between 130 and 160, the mild hypertension being due possibly to a transfusion reaction developing just before operation and persisting during this time The pulse rate remained about 120 and there was no post-operative fall of blood pressure ★

Two other patients anaesthetized only with 'Pentothal" lost larger quantities of blood externally at operation They had sustained similar traumatic amputations of a foot and, at operation under similar amounts of "Pentothal', suffered amputation through the lower leg

One patient (*Case I* 45) started operation with a blood volume of about 80 per cent normal and the blood loss at operation was estimated clinically as about 800 ml The other (*Case I* 51) started operation with a blood volume of about 75 per cent normal, and blood loss at operation was estimated roughly as 500 ml In both the haemorrhage at operation occurred chiefly during the ligature of vessels in the amputation stump after the removal of the tourniquet, and the amounts lost were roughly comparable In both the blood pressure fell, in the first from 100 to 90 and in the second from 125 to 110, in both it returned to its previous levels within 20 min as a result of further transfusion and arrest of haemorrhage

The importance of the level of blood volume during operation is clear, and it is evident from the following examples that if the blood volume is maintained at operation above the critical level, at about 80 per cent or more, these patients pass through operation with no more than unimportant and transient falls of blood pressure This holds true irrespective of the degree of tissue damage, even if this is very large, and of whether or not they have initially displayed marked circulatory collapse

★*Cases I* 45 and 53 both had moderate wounds, their initial blood losses were 55 and 50–60 per cent and their initial blood volumes 60 and 48 per cent respectively In both, the collapsed circulation was restored by transfusion, and they reached operation with blood volumes of about 80 and 77 per cent normal respectively Transfusion was continued slowly at operation In both the blood pressure was maintained above 100 at operation and subsequently

There are two other patients, both with large wounds, whose initial blood losses were 30 and 45 per cent One (*Case I* 88), who received no transfusion, reached operation with a blood volume of 80 per cent (initial blood loss 30 per cent) and, *in spite* of considerable manipulations, showed only a slow fall of systolic blood pressure throughout operation The pressure was 90 at the end of operation and recovered *without* transfusion In the other (*Case I* 81), who reached operation with a blood volume of about 70 per cent (initial blood loss 45 per cent), manipulation caused the blood pressure to fall to 80 It was soon restored by further transfusion ★

Case I 83 had large wounds and an initial blood loss of about 55 per cent of his total blood, and *Case I* 93 very large wounds and a blood loss of about 60 per cent Patients with blood loss of this order have in the past shown a high mortality from what has been called 'shock' and tended to die before, during or in the first few hours after operation It will be seen from the histories that in both these cases there would seem to have been ample opportunity for the absorption of products of damage to muscle, estimated as at least 3 hands, and other tissue Yet both passed through operation well, though the one with the blood volume nearer the critical level (but the smaller tissue damage) showed a mild hypotension which passed off soon after operation

Case I 83, a soldier aged 23, was seen 7 hr after a mortar bomb had caused compound fractures of the right femur, tibia and humerus, lacerations of the right thigh and arm and a small puncture wound of the chest wall leading into the liver At operation this wound was treated only by excision of its edges Total tissue damage was estimated as 3–5 hands, there was no evidence as to the extent of blood loss

He had already received morphine ¼ gr and ⅛ gr, one bottle of plasma and half a bottle of blood He was pale and his extremities were cold, his blood pressure was 130/80 and his pulse rate 112 His measured blood volume was 64 per cent of his predicted normal ★Transfusion of the first bottle of blood was continued and he reached operation 9 hr after injury, with a blood volume of 68 per cent normal He was still pale and his forearm veins were constricted, his blood pressure was 144/90, his pulse rate 136 The second bottle of blood was given slowly over 5 hr during and after operation

Operation lasted 2 hr, he was anaesthetized with 2 3 g "Pentothal Little blood was lost, and his blood volume was maintained by the transfusion at about its initial level

In the first 40 min of operation the blood pressure was about 110/70, but for the following 40 min it fell to 90 and remained at that level This fall appeared to be related to forcible manipulation of his fractures His pulse rate throughout remained at about 130, his face pale and his fingers cool The muscles in the region of the compound fracture were infected, so that there was opportunity for the absorption of the products of damaged and infected muscle ★

With further transfusion after operation, his blood pressure was soon restored to normal He was evacuated to Base on the fourth day

Case I 93, an Italian civilian aged 21, was seen 7 hr after injury by a mine which completely disorganized the left foot, fractured the lower end of the tibia and fibula and pulped the calf muscles There were also spattered wounds of the right thigh and face (total tissue damage 3–5 hands) A tourniquet had been applied and he had received morphine ½ gr Though transfused during the journey to the Casualty Clearing Station with three bottles of plasma (begun at 1½ hr after injury) his blood pressure was only 75/? and his pulse rate 148, he was cold and his face and lips were pale Two bottles of blood were transfused over 2½ hr At 7½ hr after injury, following transfusion of about half the first bottle, his blood volume was measured and found to be 54 per cent of his predicted normal Shortly afterwards he experienced a rigor, during which his blood pressure was 160 60 and his pulse rate 160 At the end of the second bottle he was still pale, his veins were constricted and his hands cool, his blood pressure was 160/100 and his pulse rate 144 ★Transfusion of the third bottle was begun (given over 40 min) and operation started at 10 hr after injury His blood volume was estimated then to be about 70 per cent normal

During the 40 min of operation little blood was lost, transfusion of the third bottle of blood was completed and that of a fourth started, so that his blood volume was increased during operation to at least 75 per cent He was anaesthetized with 1 5 g "Pentothal The injured leg was amputated through the thigh with considerable manipulation, but without hypotension developing His blood pressure fell to remain between 120 and 130 and his pulse rate to about 130, vasoconstriction persisted ★

He made good progress after operation and was evacuated to Base on the seventh day

Patients Anaesthetized Mainly with Ether

Fifteen patients were anaesthetized mainly with ether Anaesthesia was induced in ten cases with ethyl chloride, in one with "Pentothal", in two with nitrous oxide and in two with open ether In some of these cases the periods of induction of anaesthesia were considerably longer than in those anaesthetized with "Pentothal"

Analysis is in some respects more difficult in these patients than in those anaesthetized with "Pentothal" because (i) the dosage of anaesthetic used is less easily estimated, particularly with open ether administration, (ii) there is more fluctuation in the depth of anaesthesia, and (iii) difficulties in administration, particularly respiratory obstruction of varying degree, were much more common during both induction and maintenance Further, a high proportion of the patients suffered from large or very large wounds, though with varying amounts of blood loss before operation

None of these cases shows clearly the effects of ether itself on the blood pressure, but there is much evidence that the two pressure-lowering factors seen in the cases anaesthetized with "Pentothal", manipulation and further haemorrhage, are of importance, particularly when the blood volume is near 70 per cent of the predicted normal For example

Case I 40, who had not been transfused and whose blood volume was about 85 per cent at the time of operation, underwent during plastering considerable manipulation of the compound fracture of his tibia and fibula His blood pressure fell transiently from 100 to 90 and his pulse rate slowed from 120 to 100 He bled little at operation

Case I 95, with a similar injury but rather more tissue damage, showed the same picture except that the initial pulse rate fell from 130 to 100 with manipulation, but rose again rapidly to remain at 130 with a systolic blood pressure of 65 for 25 min of operation At the beginning of operation his blood volume was about 80 per cent

Both the last two cases were transfused more than they bled at operation so that, when operation ended, their blood pressures were restored

Case I 39 displays the effect of haemorrhage of about 20 per cent of the blood volume during operation He had a moderate wound of his calf muscles without bony fracture, several vessels were torn ★ At the beginning of operation his blood volume was 75 per cent and he was not transfused After 40 min of anaesthesia he lost steadily about 20 per cent of his blood volume over the next hour, his blood pressure fell from 140 to 50, the pulse rate rising 140 to 160 ★ His systolic blood pressure was restored to normal within 40 min by the transfusion of an amount equivalent to 18 per cent of his blood volume, and thereafter remained normal

There is much evidence also of the pressure-raising effect of periods of respiratory obstruction and of the fall of blood pressure on removing the mask at the end of operation

Respiratory obstruction during operation caused a rise in systolic blood pressure from 140 to 170 in a patient with a blood volume of 104 per cent, from 130 to 165 and from 120 to 150 in two patients with a blood volume of 84 per cent, from 120 to 150 in a patient with a blood volume of about 75 per cent and from 60 to 80 in a patient with a blood volume of about 60 per cent or less

In *Case I* 49, with a blood volume of 80 per cent, removal of the mask coincided with a fall of his systolic blood pressure from 120 to 110, and *Case I* 77, with a blood volume of 90 per cent, showed a similar sudden fall During operation both of these patients showed periods when the systolic blood pressure was raised to 160 and above apparently because of respiratory obstruction

Frequently two or more of these factors appear to be working together

Patients Anaesthetized with Cyclopropane

Six patients were anaesthetized with cyclopropane, four of them with this agent alone and two of them after induction with 0 5 g "Pentothal" They

include one patient with small wounds, two with moderate, two with large and one with very large, initial blood loss varied between 40 and 55 per cent of the predicted normal blood volume What has been said about the analysis of the cases anaesthetized with ether applies largely to these In the four anaesthetized with cyclopropane alone, the dosage was between 60 and 70 ml per minute of administration, in the two in which anaesthesia was induced with "Pentothal" it was rather less The depth of anaesthesia fluctuated considerably more than in those anaesthetized with "Pentothal" and in three cases there were marked difficulties in the administration, periods of respiratory obstruction and of apnoea occurring, during which respirations had to be maintained by pressure on the bag of the anaesthetic apparatus All the cyclopropane administrations were with Heidbrink's machine

Here, too, periods of respiratory obstruction raised the blood pressure and in three instances removal of the mask was associated with a fall of blood pressure of 20–30 mm Hg Manipulation of fractured limbs and haemorrhage also lowered the blood pressure, but a pressure-lowering effect of cyclopropane itself cannot be demonstrated in these patients The operative course of two of them illustrates the additive effects on blood pressure of the three factors of manipulation, haemorrhage and removal of the mask

Case I 76 suffered a double compound fracture of his left ankle and left mid tibia with small penetrating wounds of both legs, the total tissue damage was 3–5 hands At operation, after transfusion, his blood volume was about 80 per cent of its predicted normal Administration of the anaesthetic lasted 48 min and operation 10 min ★Before operation his blood pressure was 120/70 and his pulse rate 120 Shaving and cleansing the wounds did not alter his blood pressure On turning him on to his side the pressure fell to 95/60, but recovered to 105/70 within 10 min With continued operation and considerable manipulation of the fractured limb during the application of dressings the blood pressure again fell, this time to 80/50, and on the removal of the mask, whilst the dressings were still being applied, it fell to 50/? Half an hour later it had returned to 110/80 and was thereafter maintained Haemorrhage at operation was measured and found to be 310 ml , the blood volume was maintained at about its original level by transfusion during operation ★

Progress continued, he was evacuated to Base on the fourth day

Case I 85 suffered a compound fracture of his tibia and fibula with 3–5 hands of damage to the surrounding tissue When first seen he was estimated to have lost 55 per cent of his original blood Before operation, after transfusion, his blood pressure was 110/70 and his pulse rate 140 The administration of the anaesthetic lasted 76 min and operation 68 min ★ His blood volume at the beginning of operation was about 75 per cent of the predicted normal For the first 15 min his systolic blood pressure was 140, but the manipulation of the injured leg and the continuous haemorrhage, amounting to about 20 per cent of his blood volume, brought it down to 70 in the course of the next 35 min In the next 13 min , during the application of dressings and plaster and the removal of the mask, it fell to unrecordable levels He was transfused the equivalent of 7 per cent of his blood volume during operation★ and transfusion continued slowly after operation over the course of several hours, his blood pressure slowly returned to normal

Progress continued and he was evacuated to Base on the seventh day

Patient Anaesthetized with Nitrous Oxide, Oxygen and Ether

One case anaesthetized with nitrous oxide, oxygen and ether provides what is perhaps the best evidence we obtained of the prime importance of the level

of the blood volume in the development of periods of hypotension during operation The wounds were very large, very few cases with such injuries maintained a normal or nearly normal blood pressure during operation But in this patient the blood pressure did not fall materially during a relatively long operation involving bilateral amputation and much respiratory disturbance At one point, when he seemed about to die from asphyxia, it reached 90, but quickly recovered when the anaesthetic mask was removed Before operation he had lost much less blood than is usual in such cases and he was adequately transfused, so that his blood volume can be presumed to have been between 100 and 115 per cent of the predicted normal throughout operation The inference is that an enduring hypotension did not develop because the blood volume during operation was, unlike that of the other cases, close to normal

Case I 104, a soldier aged 25, received very large leg injuries by treading on a mine, the total tissue damage was over 5 hands The left foot and lower part of the leg were torn off and the tissues of the lower half of the remaining stump badly damaged There was a gross compound fracture of the right leg with extensive damage to the surrounding tissues Morphine ¼ gr was given ½ hr after injury

Seen at 3½ hr after injury, the wounds were not bleeding, nor was bleeding renewed subsequently He was thirsty, mentally clear but drowsy Face colour was obscured by dirt but his lips were well coloured There was some vasoconstriction, the radial pulse being thin ★ The blood pressure was 115/80 and the pulse rate 100 The measured blood volume was 80 per cent normal and indicated the loss of 25–30 per cent of his blood, an exceptionally small blood loss for wounds of this extent Transfusion (during which rigors occurred) of two bottles of blood (15 per cent of his blood volume) was given over the next 2 hr and he was sent to operation with a blood pressure of 145/100 and a pul e rate of 100, a pale face and cold extremities ★

Operation, begun 6 hr after injury, lasted 1¾ hr and consisted of amputation of the left leg below the knee and of the right leg above Manipulation was considerable but blood loss small, 270 ml being collected on swabs Anaesthesia, induced with nitrous oxide and oxygen, was maintained by nitrous oxide, oxygen and ether (Boyle s apparatus) ★Transfusion was continued during operation, again equivalent to 20 per cent of his blood volume

Anaesthesia was light, and the patient moved his limbs and groaned He quickly became and remained more or less deeply cyanosed, with a warm sweating skin and engorged veins For the first hour of operation there was marked hyperpnoea and hyperventilation, the respirations rising in rate to between 40 and 50 and becoming in character like those of a man at the end of an exhausting race There was also fluctuating hypertension, the blood pressure rising at times to over 200, the pulse rate remained about 160 Then, when the amputation of the left leg was completed, the respirations became gasping and shallow, cyanosis increased, the blood pressure fell to 90/50 and the pulse rate declined to 130 The patient seemed about to die from asphyxia Operation was suspended, the anaesthetic withdrawn and the table head tilted down After a pause of 5 min the blood pressure had risen to 130/50, the pulse rate was 138 and respirations were 28 He vomited After clearing out the pharynx the administration of the anaesthetic was resumed The patient quickly again became cyanosed and his respirations deep and crowing He vomited and inhaled vomitus The mask was removed and vomitus appeared from his nose Again the pharynx was cleared For the next 20 min, while the right leg was amputated, he remained cyanosed and repeatedly coughed and strained The blood pressure varied between 100/50 and 120/50 and the pulse rate between 120 and 140 On removing the mask at the end of operation the respirations quietened, the cyanosis, though persisting, became less, and he was returned to bed with a blood pressure of 100/50

and pulse rate of 120, the radial pulse being of good volume and the skin warm and sweating ★

After operation, when the bottle of blood was ended, a bottle of plasma was transfused slowly Oxygen was given and relieved the cyanosis *Bouts of coughing* continued ★His blood volume, measured again 1½ hr after operation (9½ hr after injury and after transfusion equivalent to 42 per cent of his normal blood volume) was 122 per cent normal,★ his blood pressure was 110/60, and his pulse rate 120

Bronchopneumonia and lung abscesses developed, but after a stormy course the patient recovered

Additional Remarks on Anaesthetic Agents

It is tempting to suggest that the three anaesthetic agents chiefly used in Italy have differing pharmacological reactions, which are reflected in the differing ability of patients with comparable blood volumes anaesthetized with them to withstand comparable amounts of haemorrhage and manipulation The vasodilating properties of ether and cyclopropane might be expected to predispose towards lower blood pressures and possibly to render the circulation more liable to falls of blood pressure as compared with "Pentothal" This is a point difficult to establish, for there is no method of measuring or comparing the stimuli from damaged tissue that cause lowering of the blood pressure in differing cases, and there are too few comparable cases

We can, however, consider those patients in the Italian Series without gross haemorrhage during operation who at operation had blood volumes between 70 and 80 per cent of the predicted normal, and who had fractures of the femur or tibia and fibula which were subjected to considerable manipulation at operation

Two patients (*Cases I* 86 and 95) anaesthetized with ether showed sharp and prolonged falls of their blood pressures to 70 mm Hg Two patients (*Cases I* 70 and 76) anaesthetized by cyclopropane showed gradual falls to 80 and 90 mm Hg respectively one later showing a fall to 50 on further manipulation and removal of the mask

Of seven patients anaesthetized by "Pentothal", two (*Cases I* 68 and 88) showed gradual falls reaching 90 mm Hg by the end of operation *Case I* 73 showed slight hypertension followed by a return to normal at the end of operation, *Case I* 83, with marked and prolonged manipulation, maintained his blood pressure at 90 and 95 for 70 min after a previous 50 min of operation, *Case I* 74 showed a steady fall of his blood pressure to 75 by the end of operation, two (*Cases I* 57 and 81) showed fairly rapid falls to 70 and 80 respectively (these two cases were the most comparable to *Cases I* 86 and 95, but the fall of their blood pressures was less sharp and the recovery more rapid), and one (*Case I* [illegible]), with very large injuries, showed no fall of his blood pressure at all

Thus it is possible that in patients of the type discussed above "Pentothal" anaesthesia renders the circulation less liable to falls of blood pressure with manipulation than does ether anaesthesia It would be of great interest to know the effects of "Pentothal" on patients with low blood pressure throughout operation, but in both series all such cases were anaesthetized with ether (with or without nitrous oxide) by choice of the anaesthetist concerned, possibly because of experience or hearsay of the ill effects of "Pentothal" However, the Italian Series presents no evidence to suggest that "Pentothal", if its pressure-lowering effect is minimized by careful administration, is dangerous to such patients

Course After Operation

Introduction

We now follow the further course of the patients when they were returned to bed after operation The duration of the period of observation is shown in Table 13

TABLE 13

Duration of observation after operation patients with limb injuries

		Time (days)						Total
		Less than 1	1–2	2–3	3–5	5–10	Over 10	
Italian Series	Patients	24	14	10	26	21	6	101
	Deaths	7	2	—	2	3	—	14
Home Series	Patients	20	14	10	13	23	27	107
	Deaths	7	3	—	2	2	—	14

Information is more detailed in the Italian than in the Home Series, for in the latter we were more concerned, at least at the start of the work, with the earlier periods It was soon appreciated, however, that many patients, particularly those with large and very large wounds, require as much careful watching and treatment in the first few hours after operation as before or during it

The post-operation course may be divided into earlier and later periods During the earlier period, about 12 hr in duration, the chief illness is circulatory and is due to blood loss During the later period, the illness may be dominated by the effects of fat embolism or infections, or by metabolic, erythrocytic and renal disturbances

Early Post-Operation Period

Most patients were returned to bed as soon as operation ended Some of those whose blood pressure was still low were retained in the theatre until they were judged sufficiently recovered to be moved without danger Patients taken from the theatre were laid flat in bed and covered with blankets sufficient to keep a normal man warm In cases with a low blood pressure the foot of the bed was often raised on blocks about a foot high In England the patient was often warmed, and sometimes overwarmed, by applying warm blankets, hot water bottles or an electric cradle Once the patients were settled in bed they were in general free from further manipulation, for damaged tissues were protected by plasters and splints In the first few hours they were recovering from the anaesthetic, manipulation, tissue damage and haemorrhage experienced at operation, they were subject to the effects of damaged tissue not removed from them at operation, and they were liable to further bleeding, since the

leaving open of widely excised wounds and of amputation stumps provided large raw areas that could well bleed more Many of them, especially in Italy, received further transfusions, and some showed the pharmacological effects already described

Before describing the circulatory changes we refer briefly to certain features associated with recovery from the anaesthetic and to the further amounts of blood likely to be lost during the early post-operation period

RECOVERY FROM ANAESTHETIC

Certain features of the early post-operation period are associated with the passing off of the effects of the anaesthetic agent Recovery of consciousness was most rapid after nitrous oxide or cyclopropane, the patient being conscious and able to sip water within ½–1 hr of the end of operation With ether and "Pentothal" the rate of return of consciousness varied considerably from patient to patient, in part depending on the dosage and depth of anaesthesia A few patients were conscious in the first hour, a few not until four or more hours after operation, the majority returned to consciousness between these times With both ether and "Pentothal" patients usually remained drowsy for some time after they had regained consciousness

During the return to consciousness periods of respiratory obstruction were not uncommon and caused the same effects on the circulation as those described during operation Little heed was paid to them unless they were gross, indeed, they often went unrecognized Laryngeal spasm was occasionally seen in patients recovering from "Pentothal" and from ether anaesthesia One case, brought to our notice as an example of death from "shock" with minor wounds, probably died as the result of respiratory obstruction after operation It illustrates not only the difficulty of obtaining adequate information about such cases of "shock" but also the need for the careful watching of patients, not always possible in the exigencies of war, in the early post-operative period

Case I 4, a soldier, aged 22, died about 2 hr after operation, begun 10½ hr after wounding and lasting about 20 min , the anaesthetic agent used was 1 25 g 'Pentothal His wounds, caused by a mortar bomb, were two small punctures in the buttock, penetrating muscle only and producing very little tissue damage or sign of bleeding, the total tissue damage was less than ½ hand The wounds were excised at operation He had received morphine ¼ gr soon after wounding and two injections of anti gas gangrene serum, the second intravenously Just before operation he was given a further injection of morphine ¼ gr and atropine $\frac{1}{100}$ gr His general condition was good

Operation necessitated turning the patient on his front, the airway was clear ★After operation he was turned again on his back, respiratory obstruction from the tongue followed Gross obstruction persisted whatever the position of the head, but an oral airway gave free breathing The patient was sent to the ward, the airway remaining in place The orderlies taking him to the ward returned 10 min later, bringing the airway with them The orderly receiving the patient in the ward said he was very pale He snored loudly when the airway was removed, but after a time his breathing quietened down The orderly was busy and only saw the patient from time to time He remained unconscious and very pale and his pulse could hardly be felt Shortly afterwards he was found to be dead ★

Necropsy 6 hr after death showed a well-developed young man with some cyanosis of the face and ears No other wounds were discovered than those noted above The

body was not exsanguinated and the organs were healthy Larynx, trachea and main bronchi contained some frothy mucus, no haemorrhages were found in brain, pleura, pericardium or lung substance

Vomiting was common during and after the return of consciousness In the unconscious patient, inhaled vomit rarely caused marked respiratory obstruction, though it might produce marked transient changes in the blood pressure and pulse rate

Some degree of restlessness was not uncommon in the return of the patient through the excitement stage of anaesthesia to consciousness, and was often controlled by injection of morphine Occasionally the restlessness associated with gross blood loss and low blood volume was mistaken for this post-anaesthetic restlessness and was treated merely with morphine In the following example from the Italian Series, examination of the blood pressure, pulse rate and extremities would have corrected this error

Case I 19, a soldier aged 25, received multiple small peppering wounds of the backs of his legs, one of which pierced the popliteal artery, the total tissue damage was less than 1 hand

During operation, 8 hr after injury, when the popliteal artery was ligated, he bled considerably He became cold, very pale and pulseless, and sweated The forearm veins were hard to find Transfusion of one bottle of blood under pressure was begun and he was returned to bed unimproved ⋆Transfusion was not continued beyond the first bottle (about 7 per cent of his blood volume) He came round from the anaesthetic (probably "Pentothal'), became very restless and complained of great thirst He was given morphine $\frac{1}{4}$ gr and suddenly became quiet At $\frac{3}{4}$ hr after operation he was quiet, pale, cold and pulseless at the wrist, his carotid pulse rate was 140, his blood pressure 40/20, his bandages were bloody After a further $\frac{3}{4}$ hr his condition had not changed In the next 3 hr he was transfused three and a half bottles of plasma and two and a half of blood, which, with an injection of ' Veritol" and rigors, raised the blood pressure to 80/60 and the pulse rate to 150 After a further half bottle, 15 hr after the end of operation, the blood volume was measured and found to be 68 per cent of the predicted normal, the blood pressure was 95/60, the pulse rate 140, and the extremities were warm His circulation subsequently returned to normal and he was evacuated to Base on the fourth day ⋆

FURTHER BLOOD LOSS

Variable amounts of blood or serum may be lost by oozing from the wound surfaces in the first 48 hr after operation, occasionally free bleeding occurs Our observations are deficient in this respect and few quantitative data are available because of the difficulties associated with blood and serum loss into dressings, plasters and bed In the Home Series the notes record free bleeding in only two cases and continued oozing in three others In the Italian Series one case bled about 250 ml into the bed and in many others the plaster or bandages were discoloured, sometimes badly, in one they were soaked with blood Since dressings were for the most part well padded with cotton wool before the application of bandages or plaster, considerable amounts of blood or serum could be soaked into them before staining would show on the surface At necropsy, stumps might be free from blood, or the dressings might be soaked through It is thought that where wounds were large or very large the loss during the first few hours after operation was not usually

more than about 250–500 ml blood and serum Such a loss, however, might be dangerous in patients with a blood volume near the critical level

CIRCULATORY CHANGES

Most of the patients in both series were returned to bed after operation warm and with a good facial colour, their pulse rates were fast, rates of over 130 being common, in about a quarter the blood pressure was under 100

In following the circulatory changes in this stage, emphasis is laid on the level of the blood pressure, for, as in the earlier stages, this provides the best index to the patient's state However, before discussing blood pressure we deal briefly with the other circulatory features

Pulse Rate

The rapid pulse rates after operation were due to a combination of factors, low blood volume, transfusion and anaesthetic agent Normally they tended to fall in the first 24 hr , but in some cases other factors, such as the development of infection and shortage of red cells, might appear at this period and maintain the fast rate The rates were faster in the Italian Series than in the Home, probably because of the larger number receiving transfusion, as well as the lower age in the Italian Series

Face Colour and Extremity Temperature

In cool and cold weather the onset of cutaneous vasoconstriction was common in the first 2 hr after operation In some instances it was associated with shivering, which sometimes became so intense as to render blood sampling difficult It was seen after all the anaesthetic agents used, and usually a combination of factors, such as heat loss during operation, reduced blood volume and the effects of transfusion, was responsible But it also occurred in untransfused patients with small wounds and normal blood volume, where heat loss during operation and the passing off of the anaesthetic agent seemed to be the factors mainly responsible The vasoconstriction usually passed off after an hour or two and was replaced by vasodilatation

Whereas in the pre-operation stage cutaneous vasoconstriction was closely associated with a low blood volume, in the early post-operation stage this was not so, since many patients with reduced blood volumes did not show a marked vasoconstriction in their extremities The hands might be warm and the forearm veins relaxed although the blood volume was in the region of 70 per cent of the predicted normal, the face might be pale or flushed Thus, for example, 4 hr after operation *Case I* 109 had warm hands, a pale face and a blood volume of 66 per cent normal, while *Case I* 43 had warm extremities, a well coloured face and a blood volume of 69 per cent normal

Level of Blood Pressure

The evidence now to be discussed shows that, whatever the changes in the other circulatory features, (1) in the great majority of patients returned to bed with a blood pressure of at least 100, the further course is uneventful, whether or not the blood pressure has been low before or during operation,

(ii) many of those returned with a blood pressure under 100 mm Hg pass through a difficult period and a high proportion die, (iii) a normal blood pressure after operation usually indicates a blood volume not below the critical level of 70 per cent normal while a persistently low blood pressure usually indicates a blood volume about or below 70 per cent normal, (iv) exceptionally, a normal blood pressure may be maintained after operation although the blood volume is a little below 70 per cent, or a low blood pressure may persist when the blood volume is well above this level, (v) a low blood pressure is restored to normal by further transfusion, (vi) in cases with a low blood pressure, failure to transfuse or to transfuse adequately may result in early death

To discuss the evidence we divide the patients into three groups according to the level of the blood pressure before and during operation

(1) those in whom the blood pressure had remained at 100 or over before and during operation, except for minor and transient falls (41 per cent of the total 80 cases, 39 Home, 41 Italian),

(2) those in whom it had previously been low but had risen to at least 100 by the time the patient was returned to bed (29 per cent of the total 56 cases, 34 Home, 22 Italian),

(3) those returned to bed with blood pressure under 100 (the remaining 30 per cent 57 cases, 31 Home, 26 Italian)

Patients with Normal Blood Pressure

Most of the patients in whom the blood pressure had previously remained at 100 or over both before and during operation had small wounds and had not lost much blood Only a few patients of the Home Series, but about half of the Italian, had received prophylactic transfusions before or during operation, transfusion was continued after operation in few

The early post-operation course was uneventful in the great majority, the blood pressure being maintained in all but three

The data are scanty and the cause of the blood pressure depression in these three is not clear In two of them the hypotension was slight, the pressure did not fall below 90 and there was vasodilatation and a well coloured face Both soon recovered without transfusion

In the third the fall was greater and accompanied by vasoconstriction, but circulation was soon restored by transfusion

Case H 70, a man aged 50, had a leg torn off through the knee by a bomb splinter in an air raid (tissue damage 2–3 hands) Amputation through the thigh was carried out under oxygen and ether, with very little blood loss, previous blood loss was judged to have been less than about 20 per cent of his blood volume and no transfusion had been given

★He returned from the theatre "in good condition', warm and with a good colour and a pulse rate of 110 He was left under an electric cradle for 2¼ hr while other cases were dealt with After this interval he was very pale and sweating and had cool extremities, the blood pressure was 60/40 and the pulse rate 130, he was mentally alert and very anxious ★ The cradle was removed and two bottles of plasma were given in 40 min By then the blood pressure had risen to 105/60 and the pulse rate declined to 112, his extremities were warm and he soon fell asleep

In the Italian Series the blood volume at the end of operation was measured or can be calculated for 22 patients It was above 80 per cent in 17, above 70 per cent in 20, and about the critical level in 2

In one of these two (*Case I* 33) it was about 70 per cent, he had not been transfused, and showed no disturbance of his blood pressure (110/50) or pulse rate (80), but he became very pale and cool immediately after the end of operation In the other (*Case I* 55) it was about 67 per cent and he was transfused with one bottle of blood after operation He was not observed in detail, but 2½ hr after operation his blood pressure was 115/75 and his pulse rate 108, and he was warm and sweating

One of the Italian cases (*Case I* 49) is thought to have bled considerably after operation, for his plaster became saturated with blood In spite of a fall of blood volume from 78 per cent at the end of operation to 69 per cent 1½ hr later, his blood pressure did not fall, though his pulse rate increased and he showed vasoconstriction

It is of interest to note also that one case (*Case I* 22) had experienced at operation 170 min of deep ether anaesthesia (stage 3, planes 3 and 4) He showed no post operative fall of blood pressure, his blood volume at the end of operation was about 80 per cent

Four of the five cases of both series which come into this group had large and one had very large wounds All five received prophylactic transfusions and, in spite of extensive tissue damage, maintained their circulation The inference is that the blood pressure was maintained because the blood volume was above the critical level

Thus in the single patient of the Home Series with large wounds (*Case H* 108) the initial blood volume may well have been about 70 per cent of normal He received transfusion before and during operation (at which little blood was lost) equivalent to about 10 per cent, and after operation to about a further 10 per cent, of his normal blood volume

The blood volumes of the three patients with large wounds in the Italian Series are calculated to have been at the end of operation 90 (*Case I* 77), 80–85 (*Case I* 84) and about 76 per cent (*Case I* 88), in the case with very large wounds (*Case I* 104) it was about 115 per cent

Patients with Blood Pressure Previously Low

The majority of patients whose blood pressure had, after being low either before or during operation or both, become at least 100 when they were returned to bed, had moderate or large wounds and had lost much blood before or during operation Almost all in both series had been transfused, and transfusion was continued after operation in half of both the Home and Italian cases

As in the previous group, the early post-operation course was uneventful in the large majority The blood pressure was maintained in all but six, in four of whom, all with moderate wounds, the fall was slight, no more than to 90 In all the blood pressure soon recovered to normal and was maintained

In three of them the data are insufficient to determine the cause of the mild hypotension In the fourth the fall was associated with the dilator phase of a transfusion reaction, the blood volume was above the critical level

This patient (*Case I* 70), who had moderate wounds of the legs and whose low blood pressure had been restored by transfusion, developed a severe transfusion reaction at the end of operation (amputation of the right leg and excision of other wounds), *the blood volume was calculated to have been about 80 per cent normal Just

before he left the theatre, during a rigor, the blood pressure was 110/60 and the pulse rate 200, he was pale and his nose cold In the ward, 10 min later, the rigors continued, the blood pressure was 100/60 and the pulse rate 164 The transfusion was stopped and hot bottles were applied During the next ½ hr, the rigors ceased and the blood pressure fell to 90/64, the pulse rate remained at 164 and his nose was still cold ★ He was not seen again for 7 hr, by which time the blood pressure was 115/70 and the pulse rate 120, he was warm and of a good colour Circulation was thereafter maintained

In the remaining two patients the fall was more serious, one of them died Hypotension was due to renewed bleeding in one and to insufficient transfusion and wound infection in the other

Case H 114 had very large wounds with much blood loss and was transfused before and during operation (p 49) Her blood pressure at the end of operation (amputation through the left upper thigh) was 105/50 and her pulse rate was 160, she was covered with an electric cradle while the remainder of a bottle of blood was transfused slowly ★At 1½ hr after operation she was pale and warm, her blood pressure was 65/40 and her pulse rate 150 The blood pressure was unchanged ¾ hr later, it was then noticed that she had bled considerably from her wounds ★

The cradle was removed, the foot of the bed raised, the wounds repacked and another bottle of blood transfused The blood pressure soon recovered to normal, and was maintained while the pulse rate dropped slowly She made good progress

Case H 74, a man aged 52, had moderate wounds of the legs received in an accident ★ Operation had been delayed till 30 hr after injury, by which time his wounds were septic He was transfused before operation but not during it At the end of the operation his blood pressure, previously low, had risen to 110/? and his pulse rate was 130 (The blood pressure was probably raised by an injection of "Veritol" given earlier in the operation)

After operation he was kept in the theatre for 1 hr in case he should collapse, but his blood pressure was maintained Shortly after his return to bed his blood pressure had fallen to 80/?, his pulse rate was 140, he was very pale, his body was hot and his nose cold His blood pressure remained low, and he was left untransfused till about 18 hr after operation ★ Then two bottles of blood and one of plasma, given over 4 hr seemed to improve his condition for a time, his blood pressure rising to 105/? He remained pale and his nose cold At 30 hr after operation he was found dead There was no necropsy

In 20 of the Italian Series who come into this group the blood volume at the end of operation was measured or can be calculated It was 80 per cent normal or more in 7 and between 70 and 80 per cent in 11 In 2 cases only was it under 70 per cent, both were transfused rapidly before leaving the theatre and in both the circulation was quickly restored and maintained

In *Case I* 57 bleeding and manipulation during operation had caused a marked fall of the blood pressure At the end of operation, when the blood volume was about 68 per cent, he was very cold, pulseless at the wrist and vomiting, and had some degree of respiratory obstruction, his blood pressure was 105/85 The rapid transfusion of the equivalent of 21 per cent of his normal blood volume quickly improved his state

Case I 39, who had bled much at operation and whose blood volume at the end of operation was of the order of 55 per cent, showed marked vasoconstriction, his blood pressure was 50/40 his pulse rate 160 He was improved by transfusion of the equivalent of 18 per cent of his blood volume, and was returned to bed with a blood pressure of 120/60 and pulse rate of 128

It is also clear from these cases that patients who have bled much before and during operation (e g up to 60 per cent of their total blood) showed no post-operative disturbance if adequately transfused

Cases I 15 and 53, the one with small and the other with moderate wounds, are both estimated to have lost initially about 60 per cent of their blood After transfusion, their blood volumes at the end of operation were about 80 per cent (*Case I* 15) and 77 per cent (*Case I* 53) In both the circulation was maintained after operation

This group also contains a number of cases whose circulatory state was maintained after operation although they had suffered extensive tissue damage For example

Case H 115, who had suffered very large leg injuries and great blood loss, had his circulation restored by transfusion before operation (p 35) Operation, begun 4½ hr after injury under nitrous oxide, ether and oxygen, lasted 1 hr and consisted of amputation through the right mid thigh and excision of the wound of the left foot After induction his blood pressure was 125/90, his extremities were warm and he sweated ★During amputation the tourniquet slipped and at least a pint of blood was lost His blood pressure fell steeply to 65/40 and his pulse rate rose to 140, but his extremities remained warm and the radial pulse of moderate width The head of the table was lowered and transfusion speeded up In 10 min his blood pressure rose to remain about 105/70 and his pulse rate declined During operation the third and fourth bottles of blood were transfused and at the end a third bottle of plasma was started slowly

On return to the ward, 6 hr after injury, he was warm and seemed in good condition, his blood pressure was 100/65 and his pulse rate 124 Circulation was maintained At 12 hr after injury, when the transfusion of the third bottle of plasma was ended, he was pale, warm, free from pain, thirsty and with a dry tongue, his blood pressure was 140/85 and his pulse rate 96 He made a good recovery (see pp 83 and 86) ★

The inference again is that the blood pressure was maintained because transfusion had been sufficient to restore his blood volume to above the critical level

Cases I 78 and 86 both had large wounds Their initial blood volumes were 60 and 74 per cent respectively Transfused before and during operation, they reached the end of operation with blood volumes calculated to be between 70 and 85 per cent of normal Both were further transfused after operation the equivalent of 7 per cent of their predicted normal blood volumes and their circulations were maintained

In *Case I* 93 (p 52), whose wounds were very large, the initial blood volume was 54 per cent normal He was then transfused before and during operation the equivalent of 20 per cent of his blood volume and after operation, during which little blood was lost, a further 30 per cent His circulation was maintained

Patients with Low Blood Pressure after Operation

Because of their high mortality (almost 25 per cent) the cases returned to bed with blood pressure under 100 are of special importance Although over half of them, mainly from the Home Series, had small or moderate wounds, they include the great majority of all the cases with very large wounds in both series The high proportion of Home cases with the smaller injuries, and therefore smaller blood loss, is an expression of the tendency to transfuse too little that, as we have seen, was common before and during operation in the early days of the war The more generous transfusion in Italy resulted in few such cases being returned to bed with low blood pressures

Examination of the group shows that (i) some, whose blood volumes were above or about the critical level, soon recovered without transfusion, (ii) others, with blood volumes below the critical level, did not recover until transfusion was given, and if transfusion was withheld or given only after delay, slowly or in small amounts, recovery was liable to be delayed and early death to result

From the point of view of transfusion, the patients in the group fall into three categories (i) those not transfused after operation, (ii) those transfused after delay, and (iii) those in whom transfusion was continued after operation

Category (i) contains 15 cases (9 Home, 6 Italian)
Category (ii) contains 14 cases (9 Home, 5 Italian)
Category (iii) contains 28 cases (13 Home, 15 Italian)

Patients not transfused If patients were not transfused after operation, in most instances it was because it was judged unnecessary With two exceptions these patients had small or moderate wounds and most had suffered no great blood loss Most had a good facial colour, warm extremities and systolic blood pressure not lower than 80 mm Hg Usually the blood pressure had been normal before operation and returned to normal within 2 hr of the end of operation, a few, who had lost more blood, recovered slowly For example

Case H 22, a man aged 25, suffered in an air raid a compound dislocation of an ankle with laceration of the foot, a small wound in the knee and another in the scalp (tissue damage less than 1 hand) He was given morphine ¼ gr before admission 2 hr after injury He was then cool, of a good colour and mentally alert his blood pressure was 120/70 and his pulse rate 90 His blood pressure was maintained and his pulse rate slowed to 75

Operation began 3 hr after injury and lasted an hour, surgery involved much manipulation and further blood loss The anaesthetic, nitrous oxide, ether and oxygen, gave rise to periods of respiratory obstruction During operation he sweated and became paler and cooler, his blood pressure showed a large respiratory variation of about 20 mm Hg and fell gradually from an initial level of about 125/70 to 105/70, and his pulse rate increased to 105

★At the end of the operation his blood pressure fell steeply to 80/50 (? end of respiratory obstruction) and he was returned to bed The foot of the bed was raised and within ½ hr his blood pressure had returned to 95/55 and the pulse rate was 93, he was warm, of a good colour and no longer sweating His blood pressure soon returned to normal and remained there ★

Case H 39, a man aged 28, received a comminuted fracture of the upper end of the tibia in a mine accident (tissue damage less than 1 hand) The leg was greatly swollen and tense from blood escaping from the severed popliteal artery Seen 6¾ hr after injury, he was mentally clear, pale and thirsty, and his hands were cool The blood pressure was 130/55 and the pulse rate 66, circulation was maintained until operation 8 hr after injury The anaesthetic agents were ethyl chloride and ether and the operation lasted 1 hr, the leg being amputated through the mid thigh with considerable manipulation ★During exploration of the popliteal space the blood pressure fell, at the end of the operation it was 95/50, while the pulse rate was 140

Half an hour later the patient, in bed and still unconscious, was warm and pale, his blood pressure had fallen to 75/45 and his pulse rate was 124 The blood pressure then gradually recovered, reaching 110/70 by 6 hr after operation, and was maintained ★

The blood volume at the end of operation can be calculated for four patients of the Italian Series In two of them it was well above the critical level

Case I 2, with small wounds and little blood loss, reached the end of operation with a blood volume of 100 per cent normal He remained warm and of a good colour, but his blood pressure fell to 90 at the end of operation, apparently because of the rapid injection of Pentothal , it returned to normal in 20 min without transfusion

Case I 23 (see p 26) had lost about 50 per cent of his blood from a compound fracture of the maxilla and had been transfused and then undergone 100 min of light and difficult anaesthesia (from a mixture of Pentothal , ether, chloroform and cyclo propane) in which there was considerable respiratory obstruction

At the end of the operation (excision of the wounds and tracheotomy) his pulse rate remained at 160, which had been its average value throughout operation, and his blood pressure fell to 70/40 He was sweating profusely, his extremities were warm and his face was flushed Sweating ceased, but he remained flushed, and he was watched in this state for 2 hr ★At the end of this period he was put to bed and thereafter, without transfusion, his blood pressure rose and his extremities became cooler His blood volume at the end of operation is calculated to have been between 80 and 85 per cent normal Good progress was maintained ★

In the other two the blood volume was just below the critical level, between 65 and 70 per cent In both the circulation slowly recovered without transfusion, though both later received blood transfusions because of low haemoglobin levels

In *Case I* 79 (large wounds), whose course during operation has already been described (p 46), the blood pressure fell abruptly at the end of operation to 35/? while the pulse rate remained at 160 His head was tilted down, but he was not transfused An hour later he was warm his colour was fairly good, his blood pressure was 70/45 and his pulse rate 124 His blood pressure gradually returned to normal and his pulse rate fell to 100 without transfusion

Transfusion was withheld for other reasons from two patients, one with large wounds and the other with very large wounds, both in the Italian Series Both cases soon died

Case I 105, a soldier aged 26 received very large wounds from a mine Both feet and the lower part of the right leg were mangled, the left thigh and buttock and perineum were grossly lacerated and the symphysis pubis separated (tissue damage over 5 hands)

Seen 1½ hr after injury, he was very restless, very cold and pulseless, and his blood pressure was unmeasurable Bleeding continued After some difficulty in entering the greatly constricted veins, three bottles of blood were transfused in ½ hr and raised his blood pressure to 80/? 60, rendering the radial pulse palpable at a rate of 150, the forearm veins were less constricted On the way to the operating theatre the transfusion needle became displaced from the vein after another half bottle had gone in, his blood pressure fell to 60/? and the veins again became constricted

★In the theatre difficulty was experienced in inserting a needle into a vein and when transfusion was restarted it would run only slowly his blood pressure became unrecordable and his pulse impalpable Meanwhile anaesthesia was induced, 2 hr after injury, by ethyl chloride followed by ether through an Oxford vaporiser Closer examination of the wounds showed them to be surgically untreatable and at 2½ hr after injury both operation *and transfusion were abandoned* The patient died ½ hr later ★

Necropsy revealed no other injuries beyond those noted above, except some retro peritoneal bleeding in the pelvis the organs were healthy Histological examination

revealed many fat emboli in the lungs but none in the kidneys, the brain was not examined

Case I 87, a soldier aged 20, sustained large wounds from a mortar bomb The left elbow and right knee joints were smashed and there were small penetrating wounds of both feet, the tissue damage was 3–5 hands From his wounds, the large amount of blood on his clothes, and his clinical state it seemed probable that he had lost about 50 per cent of his blood by the time of admission Morphine ¼ gr was given orally 3½ hr after injury and ¼ gr intravenously at 6 hr

Seen 8½ hr after injury he was cold and pale, thirsty and mentally clear, the blood pressure was 60/40 and the radial pulse barely palpable One bottle of blood, whose transfusion produced rigors, raised the blood pressure to 80/50 and made the pulse rate become measurable at 110 The second bottle of blood caused severe rigors and raised the blood pressure to 110/55, the pulse rate to 128 At 10½ hr after injury, when a quarter of the third bottle had been given, he was comfortable and his colour was improved, his blood pressure was 110/75 and his pulse rate 92 Papaverine ½ gr and scopolamine $\frac{1}{150}$ gr were given intravenously

Operation, begun 11 hr after injury, lasted 3 hr under nitrous oxide, ether and oxygen The right leg was amputated above the knee, the left elbow treated conservatively and the foot wounds excised Blood loss during operation was assessed as not more than 200 ml The remainder of the third bottle of blood and one bottle of plasma were given slowly over 2¼ hr His blood pressure, initially 120/70 (pulse rate 120), fell gradually and after 2½ hr reached 60/?, the radial pulse was impalpable and the heart rate 144 ★The second bottle of plasma and half of the third, given in ¼ hr, raised the blood pressure to 85/?, the radial pulse became palpable and its rate was 130 He was returned to bed in this state, transfusion was not continued

At 8½ hr after operation he was seen to be very ill He had just been given two injections of Coramine and was receiving oxygen by mask He was comatose and his respirations were periodic The forearm veins were not visible, the blood pressure was 80/?, the pulse rate 130 There was no gross swelling or odour of the wounds to suggest renewed bleeding or infection The blood pressure fell steeply, respirations became infrequent and gasping and the patient died in ½ hr, 9 hr after operation and 23 hr after injury ★

At necropsy, 2½ hr after death, the wounds looked clean There was some blood-stained froth in the main bronchi, and the lungs showed scattered haemorrhages and collapse of the posterior part of the right lower lobe Microscopical examination revealed many gram positive bacteria resembling pneumococci in many alveoli of both lungs upper and lower lobes, the interval between death and necropsy was thought to have been too short to have allowed much bacterial growth The other organs revealed nothing of note A moderate number of fat emboli were found in the lungs, a few in the kidneys but none in the brain

Patients transfused after delay Most of the patients transfused after delay had large or very large wounds and seemed ill at the end of operation, with blood pressures under 80, fast pulse rates and cutaneous vasoconstriction None improved till transfused, but in all except two who died circulation recovered sooner or later The blood volume at the end of operation can be calculated for two of the Italian cases, in both it was about 70 per cent normal

In some transfusion was known to be needed immediately after operation, but was delayed for various reasons, such as lack of transfusion fluid and difficulty in entering constricted veins

Case H 82, a man aged 33, had one leg severed through the thigh in an air raid and suffered tissue damage of 2–3 hands He had lost much blood before and during operation and became very ill towards the end of operation, blood transfusion was running badly

★After the end of operation, when he had recovered from the anaesthetic, he became very pale and pulseless, sweated, and lay motionless and unresponsive The bottle of blood was nearly empty and no more was available, plasma was not obtained until ¼ hr had elapsed Oxygen was administered by mask without improvement and the observer expected the patient to die Plasma was then transfused rapidly and in 15 min there was a remarkable change, the blood pressure becoming 135/70 and the radial pulse of good volume, its rate 120, the patient conversed normally★ Transfusion was continued and circulation maintained

He later developed signs of pulmonary infarctions but recovered

Case I 58, an Italian civilian aged 40 suffering from moderate leg wounds, in whom haemorrhage and manipulation had caused a profound fall in blood pressure during operation, had a blood pressure of 60 and a pulse rate of 160 and showed marked vasoconstriction at the end of operation At this time his blood volume is thought to have been 70 per cent normal or less ★The veins were greatly constricted and difficult to enter, and 70 min elapsed before transfusion could be started At this time he was pale and restless He had come round from the anaesthetic (ether) and was very thirsty, his respirations were deep, his blood pressure was 80/60 and his pulse rate 120 Transfusion of 24 per cent of his blood volume restored and maintained his circulation Good progress continued ★

In the others the gravity of their state after operation was often not recognized and they were left untransfused for periods up to 18 hr The lack of transfusion allowed them to become dangerously ill, most were then restored by transfusion, but two died *Case I* 19 (p 59) is one example, others are as follows

Case I 11, a soldier aged 30, whose general pre operative condition was said to be good, suffered from small multiple wounds of the legs and arms He was thought to have lost little blood and was given morphine ⅜ gr over the 6½ hr before operation At operation he was given a total of 1 5 g Pentothal and there was considerable difficulty with his respiration, which became mainly abdominal and jerky, and since he developed cyanosis for periods, was probably obstructed The small wounds were excised with a blood loss of about 500 ml When he left the theatre his respirations were still jerky and abdominal ★ Because his wounds were small he was sent to the evacuation ward for immediate evacuation, and there he again developed marked cyanosis and was given oxygen

At 3 hr after operation he had a rapid pulse, a systolic blood pressure of 60 and cold extremities, he was cyanosed and seemed near death After transfusion of two bottles of plasma his circulation and respiration were restored to and remained normal ★

Case I 94, a soldier aged 35, was injured by a mine in the snow-covered mountains of the Gothic Line in midwinter and did not reach hospital till 19 hr after injury, during much of which time he was exposed to great cold

On admission his pulse rate was 120 and his blood pressure 65/? Before operation he was transfused approximately 22 per cent of his blood volume, which restored his blood pressure to 128/75, and during operation he was given a further 13 per cent of his blood volume He had considerable injuries to his right calf and thigh, which were infected with gas gangrene, and a comminuted fracture of his tibia (very large wounds)

At operation his right leg was amputated through the lower thigh and his thigh wound widely excised ★At the end of the operation he had a low blood pressure and a rapid pulse

By 10 hr after operation he had not recovered from his anaesthetic It was reported that his breathing had been bad, and that his pulse had sometimes been palpable and sometimes not

At 11 hr after operation he seemed on the verge of death He was deeply comatose, his pulse was impalpable and his blood pressure was 40, his respirations were periodic He was transfused with two bottles of glucose saline and one bottle of blood in 1 hr, and subsequently with one bottle of blood and two of glucose saline, given slowly He improved greatly and recovered consciousness, and his circulation was restored ★

Subsequently he developed anuria for a period, succeeded by marked renal disturbance, from which he gradually recovered

Delayed and inadequate transfusion seem responsible for the two deaths, in one case (*Case I* 71), however, the picture was complicated by fat embolism

Case H 103, a man aged 52, received large wounds in an air raid and lost much blood Both legs were torn off below the knees and the back of both thighs lacerated (total tissue damage 3–5 hands) Tourniquets were applied above the knees soon after injury

On admission to hospital, 1 hr after injury, he was mentally alert, in great pain, very pale, pulseless, cold and sweating, and had sighing respirations, his blood pressure was unmeasurably low, his heart rate 112

He was given morphine $\frac{1}{3}$ gr and one bottle of plasma was transfused over a period of $\frac{1}{2}$ hr, his blood pressure then was 55/? and his pulse rate 120 A further dose of morphine $\frac{1}{6}$ gr was then administered and one bottle of blood transfused over the next 6 hr During this period he became warmer, but Cheyne Stokes respirations developed and persisted until operation although oxygen was given by mask At the end of transfusion, 7 hr after injury, his blood pressure was 70–80/50 and his pulse rate 132 The lower systolic blood pressure was that during apnoea and the higher during hyperpnoea One bottle of plasma was then given slowly and the blood pressure rose to remain about 100/60, his pulse rate was 120 and he became warm and sweated Occasionally he vomited Atropine $-\frac{1}{60}$ gr was given before operation

Operation, which was begun at 16¼ hr under 'Pentothal", nitrous oxide, ether and oxygen anaesthesia, lasted 1 hr, both legs were amputated above the knees Normal respiration was restored during operation His blood pressure rose initially to 120/80 but fell to reach 75/50 by the end, his pulse rate increased to 140 ★ No transfusion was given

After operation Cheyne-Stokes respiration returned At 1½ hr after operation his blood pressure was 80/50 and his pulse rate 140 At 7½ hr he was very restless and in pain, his blood pressure was 70/? and his pulse rate 140 He was given morphine $\frac{1}{6}$ gr, and 20 min later a further $\frac{1}{6}$ gr Blood transfusion was then started into a leg vein, but would only run slowly After half a bottle of blood had been given, 9½ hr after operation and 27 hr after injury, the patient died ★

Necropsy revealed no cause for death other than his injuries, the amputation stumps, brain and heart seemed healthy

Case I 71 had moderate leg injuries and his low blood pressure was not restored by transfusion He developed cyanosis and rapid laboured respirations (p 36) Operation, lasting ¾ hr, was begun at 5 hr after injury under "Pentothal" and open ether, anaesthesia was smooth and light Respirations became deeper and more rapid, cyanosis was relieved, although no oxygen was given The wounds were excised and a Thomas s splint applied The blood pressure throughout was about 75/?

★At about 18 hr after operation, no transfusion having been given in the interval, his blood pressure was 80/50 and his extremities were not cold He was mentally clear but very restless He said he felt awful, but could not define the feeling more clearly The observer thought he might be developing cerebral fat embolism He was given morphine ¼ gr and two bottles of blood, he became progressively more drowsy and comatose and died 52 hr after injury ★

Necropsy revealed, in addition to the injuries, petechial haemorrhages in kidneys, heart and scalp and multiple infarct like haemorrhages and areas of bronchopneumonia

in the lungs Histological examination disclosed many fat emboli in the lungs and a moderate number in the brain and kidney

Patients with continued transfusion Most of the patients in whom transfusion was continued after operation had large or very large wounds and seemed ill after operation, with blood pressures under 80, fast pulse rates and vasoconstriction From what has been said, it will be clear that few would have recovered without transfusion Even with transfusion recovery was often slow and no less than a third died shortly after operation

Case H 61, a man aged 42, sustained large wounds of his legs in an air raid (gross compound fracture of the left leg with tearing and crushing of all the calf muscles, three large lacerated wounds about the left knee, a simple fracture of the left wrist and several small wounds of the right leg and thigh)

When he was seen at ¾ hr after injury, his clothes about the left leg were soaked with blood and he was judged to have lost at least 20 per cent of his blood He was given morphine ¼ gr and warmed by an electric cradle, but he soon became too warm and the cradle was removed At 1½ hr after injury he was mentally clear warm and of a fair colour, his blood pressure was 110/80 and his pulse rate 76, the radial pulse was thin but the forearm veins were not constricted He was suffering considerable pain and was rather restless Blood continued to ooze from his wounds

Two hours after injury, his state being unchanged, blood transfusion was started slowly and operation begun under 'Pentothal' (0 3 g), ether, nitrous oxide and oxygen The wounds were excised the arm was put in plaster and the leg was splinted Bleeding was considerable and at one point rapid, at a guess, a litre of blood must have been lost His blood pressure fell steeply to 40/?, his pulse rate became weak and its rate rose to 140, he began to sweat and his hands, previously warm became cool The table head was tilted down Blood transfusion would enter the vein only slowly probably because of venous constriction, and by the end of the 40 min operation only two thirds of the first bottle of blood had been given

★His condition seemed so bad that he was kept on the operating table in the head-down position The remainder of the blood (200 ml) and 100 ml plasma were forced in by a two way syringe and a second bottle of blood was given in ¾ hr after which his blood pressure was 90/60 and his pulse rate 114 Sweating had ceased and the hand was again warm A bottle of plasma was transfused over the next 5¼ hr Improvement continued slowly, but twice when he was returned to the horizontal position his blood pressure fell, to rise again when his head was lowered At 6 hr after operation he was transferred to a bed in the theatre, his blood pressure being 100–110/60, and his pulse rate 110 ★He was warm and of a good colour and slept at intervals A pint of glucose saline was given rectally and at 9 hr after operation, when his blood pressure was 135/85 and his pulse rate 108, he was moved to a ward Circulation was maintained thereafter The left leg was amputated on the third day, gas gangrene developed and the patient died on the seventh day after injury

Case H 111, a man aged 58, received very large wounds of the legs in a railway accident, the right leg was completely crushed from below the knee, and the foot missing, while the left foot and lower leg were crushed and mangled Much blood was lost at the accident, and on admission, 1 hr after injury, the first aid dressings were saturated with blood

He was mentally clear and in much pain, cold and sweating His face and lips were very pale and his respirations laboured (36 per min) His blood pressure was 60/50 and his pulse rate 112 The foot of the bed was raised and morphine ¼ gr injected intravenously One bottle of blood and one of plasma in 1 hr raised his blood pressure to 95/60, his pulse rate was 96, he was warmer and his colour had improved

Operation, begun at 2¾ hr under open ether, was completed in 35 min , two surgeons operating The right leg was amputated at mid-thigh, the left below the

knee, and the blood loss was considerable The second bottle of blood was transfused slowly during and after operation At the end of operation his blood pressure was 80/50 and his pulse rate 110

★When he had recovered from the anaesthetic, ¾ hr later, he was pale, cool, in pain and very restless, his blood pressure and his pulse rate were unchanged Morphine ¼ gr was given and in 10 min he became very still and his respirations slowed He began to sweat The third bottle of blood was then transfused over 1 hr Probably because of a transfusion reaction, his blood pressure rose to 130/85 and his pulse rate to 168, respirations became deep and increased from 10 to 20 per min Transfusion was then stopped His blood pressure soon fell to 85/65 and the fourth bottle of blood was started slowly, it was completed over 3¾ hr The patient did not recover He remained pale and cold, sweating and very thirsty, and became increasingly restless and finally irrational, with cold extremities His blood pressure fell and was finally unmeasurable He died 7 hr after operation, 10½ hr after injury ★

Necropsy revealed no causes for death other than his injuries

Case I 107 had very large thigh wounds with continued bleeding, transfusion was inadequate and low blood pressure persisted (pp 36 and 47) He reached operation 3½ hr after injury, very restless and with vasoconstriction His blood pressure was 50/? and his radial pulse impalpable, his heart rate was about 150

Anaesthesia was induced by ethyl chloride and maintained with ether and oxygen After anaesthetization, blood transfusion was restarted with some difficulty and went badly until the end of the 20 min operation The left leg was amputated through the upper thigh, about 300 ml blood was lost While the leg was being manipulated during amputation, his blood pressure fell steeply to become unmeasurable and his heart rate slowed to 80 ★When the amputation was completed, the patient was placed in the head down position and given oxygen Transfusion was speeded up and the sixth, seventh and eighth bottles of blood were given over a period of ½ hr His blood pressure remained unmeasurable and his carotid pulse rate rose to 160 His extremities were cold and his veins greatly constricted Transfusion of two bottles of plasma over 50 min raised his blood pressure to 80/60 by 2 hr after operation, his pulse rate falling to 136

The patient was then removed from the theatre By the time he reached the ward his circulation had again collapsed and he died 20 min later ★

Necropsy, 18 hr after death, revealed no cause for death beyond the injuries Histological examination showed a moderate number of fat emboli in the lungs but none in the brain or kidneys

When we first met such cases in England, it was thought that transfusion had been adequate to replace blood loss and that some other factor made the cardiovascular system unable to adjust itself and maintain an adequate circulation The factor was unknown, but it was considered possible, reviving an old suggestion, that noxious substances might have been absorbed from the damaged tissues into the general circulation Further experience failed to support this suggestion and revealed that inadequate transfusion was the main factor It became clear that, in patients with large and very large wounds, if transfusion is given too slowly after operation and hypotension is allowed to persist, death is likely to follow even if belated large transfusions are given rapidly On the other hand, if transfusion is given rapidly and in generous amounts immediately after operation, such patients are speedily restored The following examples from the Italian Series illustrate this point

The first, *Case I* 101, who is estimated to have lost at least 60 per cent of his blood, was transfused only 17 per cent of his blood volume before operation, this failed to raise his blood pressure appreciably Transfusion of a further

in the lungs Histological examination disclosed many fat emboli in the lungs and a moderate number in the brain and kidney

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The first, *Case I* 101, who is estimated to have lost at least 60 per cent of his blood, was transfused only 17 per cent of his blood volume before operation, this failed to raise his blood pressure appreciably Transfusion of a further

20 per cent during operation failed to raise it above 70 After operation transfusion was greatly slowed and his blood pressure, after rising to 80, declined despite further transfusion, until eventually he died Although he suffered considerable manipulation of his fractured limbs at operation, his illness and death are thought to be due primarily to instability of his circulation caused by low blood volume, which in its turn was caused by great haemorrhage and inadequate transfusion

Case I 101, a soldier aged 27, was injured when a Bren carrier overturned His wounds were very large a dislocation of the right shoulder, a compound fracture of the left femur and a simple fracture of the right, the left thigh muscles almost severed below the fracture and the femoral artery torn He was given morphine gr ½ hr after injury

Admitted 2¼ *hr* after injury, he was mentally clear, anxious, very pale, cold and restless, and the superficial veins were constricted His blood pressure was 50/40 and his pulse rate 100 At 2¾ hr after transfusion had been begun, his blood volume was calculated to be about 50 per cent normal Transfusion of two bottles of blood over ¾ hr, with rigors, raised his blood pressure to 90 58 with a pulse rate of 130 A bottle of plasma was given slowly and his blood pressure fell again to 60/40, his pulse rate was 140 Just before he was taken to the theatre, the transfusion needle became displaced from the vein after three quarters of the plasma had been given, the total pre-operative transfusion was equivalent to about 17 per cent of his predicted normal blood volume Transfusion was restarted later during operation

Operation was started at 4½ hr after injury under ethyl chloride and ether anaesthesia (Oxford vaporizer) and lasted ¾ hr The left leg was amputated through the upper thigh and the right leg splinted, little blood was lost Ten minutes after beginning the anaesthetic his blood pressure had fallen to 45/? and the radial pulse was impalpable Plasma transfusion was restarted and the remainder of the first and a second and third bottle of plasma and a third bottle of blood were given during the rest of the operation His blood pressure rose gradually to 70/40 and his pulse rate remained about 150 A fourth bottle of plasma was started and the patient returned to bed Transfusion at operation was equivalent to about 21 per cent of his normal blood volume

*Half an hour after operation his blood volume was measured and found to be 63 per cent of normal, and indicated that he had lost initially at least 60 per cent of his blood The result of the blood volume measurement was not known in time to guide treatment and it was thought he had already received enough transfusion A bottle of glucose saline was infused slowly but only 2 oz had entered the vein in the next 3 hr During this period the stump dressings became blood stained, his blood pressure fell to 40 20 and his pulse rate remained about 150 His extremities were cold and his forearm veins constricted For a time he was incoherent and very restless, struggling so violently that he was restrained only with difficulty After being given morphine ¼ gr he quietened and at 1 hr after operation lay motionless and unconscious, his respirations were infrequent and gasping He seemed near death A bottle of blood transfused in 10 min produced no improvement With the transfusion of three more bottles of blood over the next 2 hr, he regained consciousness and his blood pressure rose for a time to 60 40, while his pulse rate slowed to 120 But vasoconstriction persisted, his blood pressure again fell and he died 12 hr after operation *

Necropsy revealed no other injuries Histological examination showed many fat emboli in the lungs and a few in the brain and kidney

The second, *Case I* 98, was also much undertransfused in comparison with those that did well The patient passed through a long period of hypotension after operation with thirst and vomiting, and was temporarily blind in one eye Subsequently he developed marked renal disturbance from which he ultimately recovered

Case I 98, a soldier aged 31, was wounded by a shell explosion His wounds were very large, his left foot was badly smashed and the right mangled, there was a compound fracture of the right femur with a 12 in long laceration of the tissues, which were very dirty and smelly at operation, and the right arm had a small wound He said he had lost 'buckets of blood' and had tried to put a tourniquet on himself but was too weak to do so, he had not lost consciousness He was given morphine ¼ gr 1 hr after injury

Slow transfusion of one bottle of plasma was begun at 6¼ hr after injury and of the first bottle of blood at 7 hr At 8¼ hr, when the second bottle of blood was started, his blood pressure was 55/30 and his pulse rate 122 per min, he was pale, cold and thirsty, his blood volume was measured and found to be 67 per cent normal, and indicated the loss of 60 per cent of his blood At 9¼ hr the third bottle of blood was begun, his blood pressure was 75/50, he was still pale and cold and shivering a little

Operation, begun 10 hr after injury under ethyl chloride and open ether, lasted ¾ hr The right leg was amputated through the upper thigh, the left foot plastered and the other wounds excised Little blood was lost but manipulation was considerable, and his blood pressure fell to remain about 50/30 His pulse rate was 140 Towards the end of operation the transfusion of the fourth bottle of blood was begun slowly ★ The blood volume at the end of operation is calculated to have been between 70 and 75 per cent of normal

One and a quarter hours after operation he had not recovered from the anaesthetic and was still pale, but warm His blood pressure was 70/40 The radial pulse was not palpable and his carotid pulse rate was 150 Nine hours after operation his blood pressure was still only 80/60, with a pulse rate of 120 He was mentally clear and quiet, he had vomited repeatedly since operation, was very thirsty and complained he could not see with his left eye By 21 hr after operation his blood pressure had risen to 100/60 and his pulse rate was 115, he was warm but pale and still very thirsty, vomiting was less frequent and he had passed urine He still could not see with his left eye, although the pupil reactions were normal and no abnormality could be detected in the discs He was given one bottle of blood and three of glucose saline slowly, and at 33 hr after operation he was better, his colour improved but he was still vomiting occasionally and hiccupping His blood pressure was 130/80 and his pulse rate 120 ★ About 40 hr after operation he bled from his stump and was further transfused

Subsequently he developed marked renal disturbance, with a rise of his blood urea to 350 mg per 100 ml (fourth day), hypertension (blood pressure 155/95) and urea clearance 17 per cent normal (sixth day) (p 87) He recovered gradually and on the twelfth day was much better, the vision of his eye had improved, his blood pressure was 145/95, his pulse rate 102 and his blood volume 81 per cent normal.

The next two examples offer a striking contrast to those just quoted Their wounds were among the largest seen either at home or in Italy In *Case I* 110 much transfusion before and during operation deterred us from continuing transfusion after operation, but his circulatory state demanded it, and estimation showed that his blood volume was only 74 per cent normal He was therefore transfused the equivalent of a further 29 per cent of his blood volume When seen 17½ hr after injury, instead of suffering, as some feared, from the results of over-transfusion, he was in strikingly good condition and compared favourably with patients with only moderate wounds who had done well

Case I 110 received very large wounds of the legs and suffered from gross blood loss, but his circulation was restored by transfusion, after renewed bleeding and collapse he was hurried to operation (under open ether) at 3¼ hr after injury (p 33) Two surgeons operated The right leg was disarticulated through the knee and the

left amputated through *the mid calf* The thigh wounds were excised and the limb splinted and plastered Operation, from the beginning of anaesthesia to the end of plastering, occupied only 40 min, during which time the fifth, sixth and seventh bottles of blood (15 *per cent of his blood volume*) were given His blood pressure remained low, being 60/20 with a pulse rate of 160 at the end of operation He suffered considerable manipulation but little further blood loss Anaesthesia was smooth

★He was kept on the table for ½ hr while he recovered consciousness, his blood pressure rose to 80/40 and his pulse rate declined to 144 The eighth bottle of blood was given, and after the ninth had been started he was sent to the ward Two hours later, after this bottle was ended, 350 ml double strength serum was *transfused slowly* His blood pressure rose for a time and then began to fall, while the pulse rate rose He vomited whatever he drank The superficial veins were constricted We were uncertain whether or not to continue transfusion, for he had already received about 5 litres of fluid containing approximately 1800 ml red blood cells and 195 g protein, the equivalent of approximately 69 per cent of his blood volume His blood volume was therefore measured 3½ hr after operation and was found to be no more than 74 per cent of normal

Tranfusion was continued the double strength serum completed 400 ml triple strength serum and two bottles of freshly drawn blood were given over the next 3 hr Vasoconstriction gave way to dilatation, and his blood pressure rose to remain for a time at 140/80, his pulse rate fell to 120 and the respirations to 12 At the end of transfusion, 21½ hr after injury, he looked remarkably well Vomiting had ceased He had no appetite, but a great thirst, and his limbs ached In spite of all the transfusion his haemoglobin was only 62 per cent and his plasma protein 5 6 g per 100 ml He improved rapidly★ although there was obvious wasting of his tissues He passed plenty of urine, his low fever subsided He became comfortable and his appetite returned He was evacuated in good shape on the eighth day and we heard a fortnight later that progress continued to be good

Case I 108 also had very large leg wounds and gross blood loss, and his low blood pressure was raised by transfusion before operation, there was a renewed fall of blood pressure during operation (p 47), and ★he reached the end of operation with a blood pressure of 85/60 and a pulse rate of 160

Transfusion was continued with 800 ml normal strength serum over 1½ hr By this time (6 hr after injury) he had recovered from the anaesthetic, his blood pressure was 115/80 and his pulse rate 120 Circulation was thereafter maintained ★

At 19 hr he was warm, rather pale, had not vomited and was drinking much He had passed more than a pint of urine since operation and continued to pass urine freely, his blood pressure was 135/70 and his pulse rate 105, his haemoglobin was 53 per cent and plasma protein 5 1 g per 100 ml He was given three bottles of blood and at 48 hr after injury he seemed in excellent condition and was evacuated to Base His haemoglobin then was 72 per cent and his plasma proteins were [illegible] 5 g per 100 ml

Two further cases with very large wounds, one from each series, emphasize the precarious hold these patients have on life in the early period after operation and the need to watch them carefully Thinking that their circulations were restored, we did not watch them longer after operation than 7 hr in *Case H 119* and 4 hr in *Case I 106*, and both died

Case H 119 had very large leg wounds and low blood pressure, but was not transfused Operation began 1 hr after injury, his left thigh was amputated and his right leg splinted (p 48) ★He was returned to bed 1¾ hr after injury with a blood pressure of 60/40 and a pulse rate of 144 He had not been transfused up to that time

One bottle of plasma was transfused, rapidly at first and then slowly, over 4½ hr in all The plasma provoked rigors at first, and his blood pressure rose to 95/70 When transfusion was slowed his blood pressure fell to 75/50 and thereafter gradually rose, reaching 100/60 at 2¾ hr after operation His pulse rate was then 130 He was

sweating, warm and thirsty, he was given morphine ¼ gr and subsequently slept at intervals His blood pressure and pulse rate remained at about these levels for the next 5 hr He was not seen again The nursing staff afterwards reported that, [illegible] hr later, blood was oozing through the stump bandages, and that he subsequently became increasingly restless but was quietened by morphine ¼ gr His pulse became weaker and he died 12¾ hr *after operation (14 hr after injury)*★

Necropsy revealed, in addition to the injuries noted above, much blood extravasated into the tissues of the right thigh and buttock Apart from the injuries, the body was healthy, the heart weighed 300 g and there was no coronary artery disease Histological examination showed a moderate number of fat emboli in the lungs and a few in the brain and kidney

This patient is exceptional in that, in spite of his extensive injuries, his blood pressure was raised to 100 (but not above) by a single bottle of plasma, which, however, caused a transfusion reaction It is possible that he had lost less blood than is usual in such cases and that this small transfusion was sufficient to raise his blood volume near the critical level The further haemorrhage after operation may well have brought about his death

Case I 106, an Italian peasant aged 23, trod on a mine and received very large wounds of the legs, the left foot was blown off above the ankle, the skin and muscles of the left calf were torn to knee level, and much damage was done to the muscles of the right calf and thigh A tourniquet had been applied and he had received morphine ¼ gr and a bottle of plasma before admission He is thought to have lost about 60 per cent of his blood Blood continued to ooze from his wounds, the dressings when removed at operation were found to be soaked with blood

Seen 7½ hr after injury, he was unconscious, with cold extremities and no colour in his face except a faint pink tinge in his lips The veins were constricted, his blood pressure was 50/25 and his pulse rate 140 He was much improved by the rapid transfusion of one bottle of serum and two of blood (rigors) He became conscious and his blood pressure rose to about 90/? A third bottle of blood was begun and operation started at 8¾ hr after injury, lasting about 1½ hr under ethyl chloride and open ether anaesthesia The left leg was disarticulated through the knee and the wounds of the right leg widely opened up and excised Operation involved considerable manipulation and blood loss

Pre operative transfusion was equivalent to about 35 per cent of his blood volume and during operation he was given a third and a fourth bottle of blood and part of a fifth He is thought to have maintained his blood volume in the region of 75 per cent of his predicted normal In spite of this considerable transfusion, his blood pressure fluctuated in the region of 70 throughout operation and on the removal of the mask fell to 35 Transfusion continued, his blood pressure rose again and, when he left the theatre almost an hour later, had reached 80–85, with a pulse rate of 120 In bed [illegible] min later his blood pressure was 100/?35 The sixth bottle of blood was transfused slowly over about 4 hr Even so his blood pressure was unstable throughout this period, rising and falling between about 80/40 and 115/?, the pulse rate varying from 110 to 120 ★At 3¾ hr after operation his measured blood volume was 85 per cent normal, his blood pressure 90 35 and his pulse rate 108, his extremities were cool and his face was well coloured Thinking that his circulation was restored we did not watch him further It was reported that about 2 hr later he became unconscious and then pale and that his respirations varied between deep and shallow He died 11 hr after operation

Necropsy showed that the thick dressings on the legs were soaked with blood and that there was a considerable extravasation of blood into the tissues of the right thigh and leg ★Histological examination revealed a few fat emboli in the lungs but none in the kidney or brain

It is to be noted in this example that, although the blood volume after operation was 85 per cent normal, the blood pressure was unstable The further haemorrhage revealed at necropsy acting on the damaged control of circulation may well have contributed to his death

FURTHER OBSERVATIONS

Two points require further consideration first, that in some cases blood pressure may not be restored to normal even though blood volume has been raised to or above the critical level, and that such cases show cutaneous vasodilatation, second, that blood volume may be low in spite of much previous transfusion

Post-operation Hypotension with Vasodilatation

It will be noted that in some cases, e g *Case I* 19 (p 59), *Case I* 2 (p 66), *Case I* 23 (p 66), *Case I* 98 (p 73), and *Case I* 110 (p 73), hypotension and tachycardia in the early post-operation stage are associated with cutaneous vasodilatation instead of the vasoconstriction that is usual during this stage and almost invariable before operation In these cases, the blood pressure was usually between 70 and 80 mm. Hg, though lower in some (as low as 50 in *Case I* 102), but the exposed extremities were warm and the superficial veins relaxed, while the radial pulse was wide The face was well-coloured in most, though pale in some, so that the patients seemed remarkably well in spite of the hypotension, and the blood volume, measured in a number of cases, ranged from 70 per cent to normal In the majority the wounds were very large, but tissue damage was sometimes small, obvious infection was unusual. Most of these patients were seen in warm surroundings

This state of hypotension with good peripheral blood flow usually lasted only a short time, passing off as the patient recovered from the anaesthetic, but in some, particularly those with very large wounds, it was prolonged In some instances the blood pressure returned to normal without transfusion, in others hypotension persisted until further transfusion was given All the patients recovered, though two of them (*Cases I* 98 and *I* 102) suffered for a time from a renal disturbance The following two examples, both with very large wounds, illustrate this state, persisting for 6 hr in *Case I* 96 and for over two days in *Case I* 102, who was the most striking example we met In both, circulation was finally restored by transfusion, in both, as in a number of others, vasoconstrictor drugs such as "Neosynephrine" raised the blood pressure, but only temporarily

Case I 96 an Italian woman aged 41, received very large wounds of the legs from a mine explosion, her left foot was grossly lacerated and her right foot amputated, and she had a wound of the left knee, with tissue damage of over 5 hands Tourniquets had been applied after injury, and on admission 1¼ hr after her injury there was no external bleeding

Two hours after injury, following the transfusion of a bottle of serum, she was very pale, cold and restless, with constricted forearm veins, her blood pressure was 80/40 and pulse rate 112 Transfusion of two bottles of blood over 2½ hr, with a severe transfusion reaction, raised the blood pressure to 130/?40 and the pulse rate to 160 Transfusion of a second bottle of serum was started and operation begun 3½ hr after injury under ethyl chloride and open ether The administration caused

some respiratory obstruction Operation lasted 1 hr and involved much manipulation The right leg was amputated below the knee and the left above the ankle, the knee wound was excised Little blood was lost, and her blood volume throughout the operation was probably about 70 per cent She maintained her blood pressure throughout operation, perhaps in part because of the marked transfusion reaction just before operation and the respiratory obstruction due to the anaesthetic

★When the operation was finished the serum transfusion was stopped The blood pressure fell rapidly from 110/60 to 95/60 as she left the theatre and was 80/40 when she was put to bed a few minutes later The blood pressure continued to fall, reaching 60/45 2 hr after operation, at this time the radial pulse was barely palpable and its rate was 160, her extremities were warm and the forearm veins filled readily distal to an obstruction The foot of the bed was raised The blood pressure rose, to remain about 75/50, while the pulse rate declined to about 140, vasodilatation persisted When in this state, 3 hr after operation, her blood volume was measured and found to be 71 per cent normal Transfusion of one bottle of glucose saline over the next 3 hr, together with the injection of 0 1 mg 'Neosynephrine', raised the blood pressure to about 105/70 and brought the pulse rate down to 120 Then, since the blood pressure began to fall again, she was given a transfusion of two bottles of blood, which restored and maintained the circulation When the blood volume was measured again 21 hr after operation it was found to be 95 per cent normal ★ Progress was maintained and she was evacuated on the fourth day

Case I 102 had very large wounds with gross blood loss, his transfusion was inadequate, and he was sent to operation with low blood pressure (p 77) At operation, begun 5½ hr after injury and lasting ¾ hr under nitrous oxide, ether and oxygen, the right arm was amputated above the elbow and the left leg above the knee, and the other wounds were excised There was said to be little blood loss at operation A fourth bottle of blood was transfused and plasma begun Throughout operation the blood pressure remained low, only once rising transiently to 80/30

★After operation he was given continuous oxygen by mask, and 1 litre of 10 per cent glucose and 400 ml 2 per cent soda bicarbonate were transfused His blood pressure fell lower, reaching 50/? about 8 hr after operation During the next 14 hr he was given further transfusion of one bottle of blood, one of plasma and at least 1 litre of glucose saline His blood pressure rose to remain for a time about 70/50 Vomiting continued He passed 120 ml urine on one occasion

Twenty one and a half hours after operation he was mentally clear, and spoke and answered questions without difficulty He gripped a hand strongly His face was well coloured, he was sweating slightly and his extremities were hot (the ward was hot) He was a little restless and very thirsty and his tongue was dry The radial pulse was wide and soft, its rate 140, his blood pressure was 50/20 ★ There was no swelling or tenderness of the stumps, which were covered with gauze and strapping Over 2 hr he was given 1 litre [illegible] per cent glucose, to which was added 0 1 [illegible] "Neosynephrine' This raised his blood pressure to between 80 and 90 and maintained it His pulse rate slowed to 120, he sweated freely, his extremities became cooler, and he became more comfortable and fell asleep At the end of the infusion his blood pressure fell again to remain at about 55/30 and his pulse rate rose to 130 His extremities were warm

★Thirty-one hours after operation his state was the same as at 21½ *hr* He was given two bottles of blood and during the next 4 hr his blood pressure rose to remain about 90/50 with a pulse rate of about 110 Vomiting ceased and diuresis set in and the patient began to feel much better At 38 hr after operation his blood pressure was 90/55, his pulse rate 112 His blood pressure remained between 90 and 100 and his pulse rate about 100 for another 24 hr He was then given another two bottles of blood His blood pressure rose to 115/70 and was thereafter maintained, the pulse rate gradually slowing ★ For further course see p 86

The explanation of this state of long lasting hypotension with good peripheral blood flow is unknown and further observations are required

Whatever the factor or factors responsible, it seems that in some *instances* the blood pressure is restored only slowly after operation even when the blood *volume is above* the critical level and that the process can be hastened by *further transfusion* to raise the blood volume nearer the normal

This circulatory pattern of hypotension and peripheral vasodilatation recalls that provoked by general inhibition of constrictor tone (*e g high spinal* section) and by vasodilator drugs It is possible that in some of these preceding examples hypotension had damaged the constrictor control of the vessels and that in others the vessels were under the influence of a dilator substance derived from damaged or infected tissues or introduced by the transfused fluids It may be that the transfused blood had in a lesser degree the dilator effect of the abnormal blood transfused to *Case I 92, as described previously* The extreme dilatation of the skin vessels and the very low blood pressure that developed in this patient before operation persisted Unlike the others, who all recovered, this patient did not respond to further transfusion and soon died

Case I 92, who had large leg wounds, was possibly given bad blood, there was a renewed fall of blood pressure with great cutaneous vasodilatation (p 35) Operation, amputation *through the lower thigh*, was performed 9 *hr after injury* under Pentothal , nitrous oxide, ether and oxygen Throughout the operation his blood pressure and pulse rate were unmeasurable, but his skin remained brightly flushed

While in this same state after operation, the fourth, fifth and sixth bottles of blood were transfused over 5, 8 and 22 min. respectively His blood pressure could still not be measured The heart rate was 150, the radial and brachial pulses were impalpable, but the carotid and femoral could be felt easily The skin of the trunk showed a bright *pink* flush, like a punctate scarlatiniform rash, the more dependent parts (the head and neck, since he was in the head down position) were more deeply and uniformly coloured The exposed extremities were cool Colour returned very slowly when the skin was blanched by pressure The *forearm veins were not constricted*, they and the external jugular veins filled slowly distal to an obstructing finger After exposure to room air for some time, the brightly flushed skin became slightly cyanosed the bright colour returned when the skin was warmed by covering with blankets

At this time 400 ml double strength serum was transfused over 3 hr In other cases of low blood pressure this transfusion invariably provoked a strong vasoconstrictor response In this instance skin colour and the calibre of the forearm veins remained unchanged, the blood pressure was raised, for a time only, to 70/30, the heart rate remained very fast. Finally transfusion of normal strength serum was begun, but the patient died, without regaining consciousness, 17 hr after injury

Necropsy, *1 hr after death*, revealed no cause for death other than the injuries The areolar tissues were slightly oedematous, the oedema fluid being yellowish brown in colour The *intima* of the larger arteries was also stained yellowish brown The lungs were not oedematous A few fat emboli were found in the lungs but none in the kidneys, the brain was not examined

Post-operation Blood Volume and Previous Transfusion

It will have been noted, especially in the patients with very large wounds, that the blood volume after operation is often low in spite of much previous transfusion

Case I 96 (p 76), 3 hr after operation the blood volume was 71 per cent normal although previous transfusion was equivalent to 45 per cent of the predicted normal blood volume

Case I 101 (p 72), ½ hr after operation the blood volume was 63 per cent, transfusion had been 42 per cent

Case I 106 (p 75), 3¾ hr after operation the blood volume was 85 per cent, transfusion had been 65 per cent

Case I 110 (p 73), 3½ hr after operation the blood volume was 74 per cent, transfusion had been 63 per cent

A further example is *Case I* 109 quoted below This patient, although given transfusion equivalent to 65 per cent of his predicted normal blood volume, had a blood volume of only 60 per cent normal 4 hr after operation His blood pressure was then probably normal, perhaps because of previous strong rigors

Case I 109, a soldier aged 24, received very large leg wounds The whole of the left leg was smashed and the right peppered with small wounds and bruises, there was a compound fracture of the os calcis and tissue damage of 7–8 hands He had been given morphine ¼ gr after injury At operation he became very collapsed and restless, with a low blood pressure and fast pulse ★He was given three bottles of plasma and two of blood (29 per cent of his predicted normal blood volume)★

Seen 10 hr after injury, he was drowsy, very pale, cold and thirsty, and his forearm veins were constricted, his blood pressure was 120/75 and his pulse rate 150 ★Further transfusion of 23 per cent of his blood volume (three bottles of blood) was given★ and, his blood pressure being maintained, operation was begun at 12½ hr after injury under anaesthesia with open ether It lasted 1¼ hr , the left leg, found to be infected, was amputated above the knee, and the right leg was widely opened up and the damaged tissue excised There was much manipulation but little external blood loss and no serious difficulties arose with the anaesthetic His blood pressure fell and remained between 80 and 90, the pulse rate was 150–160 ★During operation he was transfused with one bottle of plasma, another, of double strength, was begun towards the end and continued after operation

His blood pressure rose slowly and 3 hr after operation reached 100/55, his pulse rate was 132 His face and lips were pale, his extremities warm The circulation was maintained His blood volume, measured 4½ hr after operation, was 66 per cent normal, he was still pale, but very hot, and his respirations were rapid and shallow He had bouts of great restlessness He was given a further transfusion of a fourth bottle of blood and during this, at 6¼ hr after operation, he was quiet, warm, still thirsty and pale, though his lips were better coloured, his blood pressure was 110/40 and his pulse rate 112 ★

At first progress was unsatisfactory Although his blood pressure was maintained, his pulse rate increased and vasoconstriction returned He bled considerably into the plaster on his leg and his wounds became septic The transfusion of a further three bottles of blood improved his state, his pulse rate slowed, the colour of his face improved and vasoconstriction passed off At 50 hr after operation his blood volume was measured and found to be 96 per cent normal At a second operation, 36 hr later, the leg was amputated through the mid calf After this he improved gradually and was evacuated to Base on the ninth day

Initially we were inclined to doubt the validity of the blood volume measurements after operation in such patients In the first place, even though generous allowance was made for blood lost by haemorrhage, it seemed very unlikely that blood volume could be so low after such large amounts of transfusion Secondly, back-calculation of the initial blood volume from the blood volume measured after operation gave estimates that seemed too low to be compatible with life

TABLE 14

Blood volumes before and after operation

Patient	Size of wounds	Blood volume before operation	Gain by transfusion between blood volume estimates	Loss by haemorrhage at operation	Blood volume after operation	Transfusion: Before post operation blood volume estimate: Blood	Plasma (bottles)	Serum	Transfusion: After post operation blood volume estimate: Blood (bottles)	Serum
		(per cent predicted normal blood volume)								
		Measured			*Measured*					
I 1	Small	118	—	<5	115	—	—	—	—	—
I 14	„	112	—	—	123	—	—	—	—	—
I 2	„	105	—	<5	100	—	—	—	—	—
I 9	„	104	—	<5	108	—	—	—	—	—
I 11	Moderate	102	—	<5	99	—	—	—	—	—
I 49	„	84	—	About 10	69	—	—	—	—	—
I 88	Large	80	—	10	76	—	—	—	—	—
I 79	„	70	—	5	64	—	—	—	—	—
I 76		74	25	About 10	77	2	—	1	—	—
I 86	„	74	24	„ 10	70	3	—	—	—	—
I 104	Very large	[illegible]	42	6	122	4	—	—	—	—
		Calculated								
I 96	„	30	45	About 5	71	2	—	2	[illegible]	—
I 101	„	23	41	Little	63	3	4	—	4	—
I 106	„ „	35	65	About 10	85	6	1	1	—	—
I 109	„ „	30	65	Much	66	5	6	—	1 (+ 3 later)	—
I 110	„ „	40	69	„	74	9	—	1½	[illegible]	1⅔

Table 14 shows that, in most of the cases in which blood volume was measured both before and soon after operation, back calculation of the pre-operation blood volume from that measured after operation gives an estimate not greatly different from that actually found Most of the cases had small or moderate wounds and no transfusion, and bled but little between the two estimations In only two of them (*Cases I* 76 and *I* 86, both with large wounds) ■ the measured initial blood volume considerably higher than the value obtained by back-calculation

In patients with very large wounds, with few exceptions, the blood volume could not be mea ured initially, back calculation gives estimates of initial blood volume ranging from 23 to 40 per cent of the predicted normal

Further experience, however, strongly suggested that the low estimates were not grossly inaccurate The clinical state of the patients, their subsequent course and the response to transfusion all indicated that they were of the correct order In fact, they provided a clear indication as to whether transfusion should be continued and how much should be given, at a time when it was difficult to reach a decision on other grounds As has been pointed out, it is important in patients with very large injuries to the limbs to raise blood volumes well above the critical level, because their circulatory control is damaged or unstable and because they may bleed further from their wounds for some time after operation, e g *Case I* 101 (p 72) and *Case I* 106 (p 75) Usually, so much transfusion has been given that further transfusion is feared as excessive, e g *Case I* 101 and *Case I* 110 (p 73) In such cases blood pressure may be a misleading index of blood volume, low blood pressure is usually associated with a blood volume in the region of 70 per cent normal or less (*Case I* 96, blood pressure 75/50, blood volume 71 per cent normal, *Case I* 101, blood pressure 65/40, blood volume 63 per cent normal, *Case I* 110, blood pressure 95/60, blood volume 74 per cent normal), occasionally with a volume well above this level (*Case I* 106, blood pressure 90/35, blood volume 85 per cent normal), and occasionally a normal blood pressure is related to a low blood volume (*Case I* 109, blood pressure probably normal, blood volume 66 per cent normal)

If transfusion is withheld from or given too slowly to such patients with blood volumes in the region of 70 per cent normal, they do not recover quickly and may die

In *Case I* 96 (p 76) the blood volume was 71 per cent normal An infusion of glucose saline and an injection of "Neosynephrine provoked only a transient rise of blood pressure, but transfusion of two bottles of blood soon restored the circulation

In *Case I* 109 (p 79), whose blood volume was 66 per cent normal, transfusion of one bottle restored the blood pressure to normal, but he remained ill until three more bottles of blood were transfused later

In *Case I* 101 (p 72), whose blood volume was 63 per cent normal, rapid transfusion was delayed till 4 hr after operation, by which time the patient seemed about to die, and it failed to save his life

On the other hand *Case I* 110 (p 73), with a blood volume of 74 per cent normal, illustrates the remarkably quick recovery that follows rapid and adequate transfusion given soon after operation

It follows from these observations that patients with very large wounds require very large amounts of transfusion. Table 14 shows the amounts given, measured in bottles of blood, plasma and serum, up to the time of estimation of the post-operation blood volume, and also the amounts given in the succeeding few hours In patients with such large wounds and massive transfusions we have seen no evidence of over-transfusion, but frequent evidence of under-transfusion. Further discussion will be found in Part IV

REMARKS

From the evidence presented it is clear that (*a*) the chief and most dangerous illness of these patients, in this period as earlier, is circulatory in origin, (*b*) it is seen in those who have bled greatly before and sometimes also during operation, and in particular in those with large or very large wounds, (*c*) it is commonly associated with blood volumes in the region of 70 per cent or less of the predicted normal, and (*d*) it can be treated by sufficient transfusion before, during and after operation, which in the cases with very large wounds may mean the contents of 12 or more pint bottles of blood and plasma or serum. In general, patients with post-operation blood volumes in the region of 80 per cent normal showed no circulatory disturbance. A few, however, showed prolonged periods of low blood pressure and rapid pulse rates, although with evidence of good blood flow through their extremities, when the blood volume was as much as 85 per cent normal, all of them recovered, some with and some without transfusion.

In this period the best guide to a much reduced blood volume is the blood pressure, which when persistently low usually indicates a blood volume in the region of 70 per cent of the predicted normal or less The pulse rate, face colour and temperature of the extremities do not help in determining if the blood volume is reduced, for instance, to 75 or 80 per cent normal, for patients with blood volumes of this order may differ little in their circulatory patterns from those with normal blood volumes

All circulatory disturbances either were continuations of disturbances arising at operation, or arose shortly after the end of operation, so that if the blood pressure was maintained in the first hour or two after operation it remained up, however it must be remembered that a blood pressure of over 100 may be caused by pressor factors such as respiratory obstruction and transfusion reactions, and so may give a false impression of the circulatory state.

The early post-operation period, particularly in those with large and very large wounds who have lost much blood, is a period of considerable danger requiring as careful attention and as skilful handling as the periods before and during operation. It is emphasised that all patients with very large wounds need watching with the greatest care for at least the first 12 hr after operation, since their lives seem often to hang by a thread. The damaged or unstable circulation on which they depend can be restored by prompt and adequate transfusion after operation.

Late Post-operation Period

The course of the patients in the late post-operation period is dealt with only briefly. Data are incomplete, particularly for the Home Series, and we do not analyse in detail. Certain of the changes occurring in the blood and urine, mentioned here, are considered more fully in Part IV.

Most of the patients both at home and abroad were given a course of one of the sulphonamide drugs over the two or three days succeeding operation; in Italy penicillin was also used, either alone or in combination with the sulphonamides. The patients were encouraged to drink freely.

CONTINUED ILLNESS

A number of patients, particularly those with the larger wounds, remained ill for a few days after operation, pale and thirsty, with dry mouths and furred tongues. They were uncomfortable and restless, slept badly and lacked appetite; some were nauseated and vomited frequently. Even in the absence of obvious infection, low fever was usual for a few days, and in some cases wasting was obvious within a week. Not uncommonly the systolic blood pressure rose to between 140 and 160, and on occasion higher, for a few hours to several days. These features were seen more frequently and more distinctly in patients of the Home Series than in those of the Italian, who were younger, in better general health and transfused more generously. Although the data are insufficient to establish the point, our impression is that adequate replacement of blood loss by transfusion in the earlier stages is an important factor in mitigating illness in the late post-operation period.

Among the patients with very large wounds who survived into this period, three stand out as making remarkably rapid progress after operation; their injuries were among the largest seen and they were transfused more than the others that did less well.

Case H 115 (p. 64) by the fifth day looked well and felt "champion"; *Case I* 108 (p. 74) was in excellent condition and evacuated to Base within 48 hr. of operation, while *Case I* 110 (p. 73) within 24 hr. of operation was remarkably well and in a state comparable to that usually seen in patients with only moderate wounds.

FALL OF HAEMOGLOBIN

In many the haemoglobin concentration of the blood fell considerably, falling particularly low in those who had lost much blood, even though much blood had been transfused. It fell rapidly at first and then more slowly, reaching the lowest level in 3–14 days after operation, after which it rose gradually. Measurement of the blood volume showed that the fall was due in part to a rapid increase in the volume of the blood plasma to normal levels or above, and in part to a continued loss of red cells from the circulation, which apparently occurred even when bleeding was arrested and obvious infection absent. These features are illustrated in Table 15, which shows the changes occurring in the 11 patients of the Italian Series in whom the blood volume was measured during both early and late post-operation periods. The

TABLE 15

Data relating to blood volumes measured in early and late post-operation periods

Patient	Size of wounds	Early post operation period								Late post-operation period								
		Time after operation (hr)	Previous transfusion (bottles)			Venous haemoglobin (per cent normal)	Blood volume (per cent predicted normal)			Time after previous blood volume estimation (hr)	Transfusion in interval (bottles)			Haemorrhage in interval	Venous haemoglobin (per cent normal)	Blood volume (per cent predicted normal)		
			Blood	Plasma	Serum		Total	Plasma	Red cell		Blood	Plasma	Serum			Total	Plasma	Red cell
I 22	Small	15	1	1	—	72	87	103	66	70	—	—	—		54	84	117	48
I 51	Moderate	1	2	—	—	92	81	78	77	23	1	—	—		76	87	102	71
I 58		14	5	—	—	81	79	89	65	72	—	—	—	Plaster blood stained	73	[illegible]	111	70
I 68		2	1	1	—	77	81	93	64	61	—	—	—		61	[illegible]	103	56
										23	2*	—	—		69	99	121	71
I 70	Large	8	1½	—	1	65	83	107	53	74	—	—	—	No gross ooze	46	[illegible]	137	45
I 84		18	2	[illegible]	—	57	74	99	44	64	—	—	—		49	[illegible]	114	40
I 85		½	4	3	—	[illegible]	73	98	43	81	1*	1	—		52	86	118	48
I 88		2	—	—	—	91	76	82	66	70	—	—	—	Fair amount of oozing	56	97	134	54
I 96	Very large	3	[illegible]	—	2	[illegible]	71	100	35	18	2	—	—		54	[illegible]	133	49
I 109		4	5	6	—	48	66	96	33	71	3*+1	—	—	Bled into plaster	65	94	120	66
I 110		4	9	—	2	69	74	88	55	64	2*	—	1	Some ooze	47	97	134	[illegible]

* Fresh blood

N B The blood volume of *I* 68 was measured twice in the late post operation period

factors controlling these changes require further investigation Further discussion will be found in Part IV

Because of low haemoglobin levels, a considerable number of patients of both series were given further blood transfusion For this purpose freshly drawn blood was preferred to stored, since, although again the data are incomplete, our impression was that it produced less frequent and less severe transfusion reactions, a greater rise of haemoglobin and more rapid general improvement

In *Case I* 110 (p 73) difficulty was experienced in finding a blood that neither agglutinated with his blood nor gave him severe reactions This is probably related to the previous massive transfusions of group "O" blood to a group 'A' patient

DISTURBANCE OF RENAL FUNCTION

In the majority of cases it was only possible to make the common routine observations on the urine, but in a number (mainly in the Italian Series), urine urea and urea clearance were estimated The only test of renal function used was the urea clearance, estimated with a urine flow of over 1 5 ml per minute, a marked diminution in urea clearance probably indicates a marked decrease of glomerular filtration

Work on renal blood flow was curtailed by the end of the war Observations on nitrogen metabolism and urinary pigments are given in Part IV (pp 294 and 295)

A disturbance of renal function was common Its chief characteristics were a delay, sometimes of 24 hr or more, in passing urine after injury, and the presence in the urine for a day or two of abnormal constituents—protein, red cells and, less often, hyaline and granular casts

According to statements by patients and ward staff, few patients in either series urinated between injury and 6 hr after operation In most cases the first urine was passed 12–24 hr after operation After this initial delay, which was unrelated to wound size or amounts of blood loss, the cases with the smaller wounds and blood loss only exceptionally showed further disturbances They continued to pass urine freely, any abnormal constituents that had been present soon disappeared and the blood urea did not rise

Case H 19, a man aged 29, who suffered only small wounds (laceration of the hand) and small blood loss, first passed urine (480 ml normal urine) 12 hr after operation, 14 hr after injury In the next 12 hr he passed a further 2 litres There was no later disturbance and the blood urea did not rise

Patients with larger wounds and greater blood loss showed further evidence of disturbance, in some cases transitory and in some prolonged There are observations on 14 patients of the Italian Series, 13 of whom had large and very large wounds In 9 there was a transitory disturbance, urine was not passed for 15–30 hr after injury, and the first few specimens contained small amounts of albumen, red cells and granular and cellular casts Their urea concentrations varied between 1 5 and 3 0 g per 100 ml , averaging 2 g per 100 ml , and the specific gravities were 1,020 or higher The two patients with the largest injuries and estimated blood loss, *I* 109 and *I* 110, both showed

such pictures, but by the sixth day after injury the urine and urea clearances were normal and the blood ureas were 40 and 36 mg per 100 ml respectively Both were Group A and had received large quantities of Group 0 blood containing anti-A agglutinins Thus it is clear that even the most grossly injured cases need not, if they receive adequate transfusion, suffer any more than temporary renal disturbance, and that the transfusion of large quantities of Group O blood to Group A subjects need not lead to any great degree of disturbance

★*Case I* 110 had very large leg injuries with 7–8 hands tissue damage, and was well transfused (pp 33 and 73) He first passed urine (about 500 ml) 16½ hr after operation, 20 hr after injury, and in the first 24 hr he passed 1,300 ml This amount was doubled in the next 24 hr and trebled by the fifth day The first urine contained protein, red cells and some granular casts, which decreased and disappeared by the fifth day The blood urea, which at 1¾ hr after injury was 40 mg per 100 ml, had risen to 166 by 21½ hr but then rapidly fell, being 36 mg per 100 ml by the sixth day after injury ★

★*Case H* 115 received very large leg injuries, with 7–8 hands of tissue damage, and was well transfused (pp 35 and 64) He had passed urine about ½ hr before injury and did not urinate again till 6½ hr after operation, 12 hr after injury The urine contained a little protein and some red cells In subsequent specimens the red cells were absent, though a trace of protein persisted for at least three days In the first 24 hr after operation, when his fluid intake by mouth was 1,100 ml, he vomited 900 ml and passed 600 ml urine In the second 24 hr his fluid intake was 1,600 ml, he vomited 300 ml and passed 750 ml urine In the third 24 hr his intake was 2,200 ml, he passed 1,500 ml urine and vomiting had ceased His blood urea remained at 35 mg per 100 ml ★

A greater degree of renal failure developed in 5 of these Italian cases, 4 of whom suffered from large or very large wounds The factors which, separately or combined, may have played a part are inadequate transfusion, mismatched or infected transfusion, a prolonged period of low blood pressure and vasoconstriction, and crystalluria from sulphonamides It is thought that the most important of these factors was inadequate transfusion

The renal disturbance of *Case I* 102, who suffered from very large wounds and probably much blood loss, was probably due mainly to insufficient transfusion of blood and plasma This patient is of considerable interest, since for a period of 38 hr his systolic blood pressure remained between 50 and 75 mm Hg, and for at least 10 hr of this period there was evidence of vasodilatation in his extremities This prolonged period of low blood pressure apparently caused no lasting damage to his kidneys

★In *Case I* 102 (pp 34, 77) very little urine was obtained in a period of hypotension which lasted in all about 38 hr (6 hr from injury to operation and 32 hr after operation) He first passed urine, 600 ml containing red blood cells, 2 hr after injury The next specimen, 100 ml containing red blood cells and casts, was obtained by catheter 8½ hr after operation The third specimen of 120 ml was passed 18 hr after operation, it was dark coloured, but was not examined Thus in the first 24 hr after operation, despite a fluid intake of about 3,500 ml (300 ml blood, 250 ml plasma and the remainder salines by vein and by mouth), only 220 ml urine was obtained, an unknown, but apparently not a great, amount of fluid was lost by vomiting Thirty two hours after operation circulation was restored by further blood trans-

fusion and diuresis set in, and in the second 24 hr after operation, when fluid intake was about 3,000 ml (including 500 ml blood), urine output rose to 2,745 ml and vomiting ceased

At 44 hr after injury his blood urea was 152 mg per 100 ml, the urine was clear and contained only a little protein and a very few red cells and hyaline casts Nine days after injury the urine was normal, his blood urea was 33 mg per 100 ml and urea clearance was 97 per cent normal ★

It is of interest to compare this case with *Case I* 91, who suffered a lesser degree of renal disturbance

★*Case I* 91, whose wounds were large and who was estimated to have lost 50 per cent of his blood, was transfused 40 per cent of his predicted normal blood volume in blood and plasma, his leg was then amputated, 18 hr after injury At the end of the operation his systolic blood pressure was 100, but thereafter declined, to remain below 70 for at least 6 and probably 12 hr During this period his extremities, like those of *I* 102, showed vasodilatation His blood volume was 85 per cent normal With further transfusion his systolic blood pressure rose to 100, and by 41 hr after injury he was passing urine containing red cells, casts and protein By the fourth day after injury the urea clearance was normal, and there was only a trace of protein in the urine ★

These two cases indicate that periods of some hours in which the blood pressure is scarcely sufficient to provide a filtration pressure in the glomeruli, when there is evidence of peripheral vasodilatation, may not result in permanent renal damage

Case I 98, who suffered from very large wounds and much blood loss, showed a greater degree of renal failure For a period of 6 hr after wounding his systolic blood pressure was 50–70 mm Hg and he showed much vasoconstriction He was insufficiently transfused before and after operation, suffered from much vomiting before operation, and was given 12 g sulphathiazole a day All these factors are thought to have contributed to the failure

★*Case I* 98 (p 73) first passed urine (100 ml containing protein and red blood cells but no casts) 19½ hr after operation, 30½ hr after injury He was then very thirsty and a little confused mentally, and was vomiting from time to time, his blood pressure was 100–105/60–70, his blood urea 144 mg per 100 ml By 36 hr after operation, after one bottle of blood, three bottles of glucose saline and 1 litre of fluid by mouth (a total of about 3½ litres of fluid), he had vomited about 1 litre and passed in all 350 ml urine In the next 24 hr there was some oozing from the amputation stump, two bottles of blood were transfused, and glucose saline was given by mouth and rectum (total fluid about 4 litres), during this period he vomited 600 ml and passed 600 ml urine No further record of intake and output was kept, but after this time he was said to have passed plenty of urine By 115 hr after injury he was still a little drowsy and mentally confused, he was very thirsty, his tongue was dry and brown, his blood urea was 350 mg per 100 ml (its peak value) At 141 hr the blood pressure had risen to 155/95 At about 164 hr the urine was normal, blood urea 250 mg per 100 ml and urea clearance 16 per cent normal

After this he rapidly improved Twelve and a half days after injury, after a bottle of blood had been transfused the previous evening he was mentally clear and cheerful, his tongue was clean and moist, his vision (which had previously been impaired) had improved and his blood pressure was 145/95 He said he was passing "pints of urine" His blood urea was 60 mg per 100 ml, and his haemoglobin was 50 per cent, his blood volume 81 per cent, and his red cell volume 37 per cent, of normal ★

Two cases, *I* 95 and *I* 67, died from renal failure which was thought to be due to the transfusion of mismatched or abnormal blood In *Case I* 95 an added factor was probably the excessive fluid intake

Case I 95, a soldier aged 34, received very large wounds of both legs from a mine Seen at 3½ hr after injury, he was very pale and cold, the radial pulse was thin and the forearm veins were greatly constricted, his blood pressure was 70/50 and his pulse rate 140 Transfusion of two bottles of blood (presumably Group O, the patient was Group A) over 1 hr, with rigors, raised his blood pressure to 115/90, his pulse rate decreased to 108 His blood volume, measured at 4 hr during the transfusion of the second bottle of blood was estimated to be 72 per cent normal, the blood lost was calculated as probably 40 per cent of his total blood These estimations were however rendered doubtful by obvious haemolysis in the venous samples

About 500 ml. blood was lost by continuing haemorrhage from the wounds, two bottles of plasma were transfused and a third bottle of blood was begun. Circulation was maintained and operation started at 6¾ hr after injury It lasted 50 min. under ethyl chloride and ether, the leg was amputated below the knee, the wounds were excised and plasters were applied His blood pressure soon fell and remained about 65/45 It is thought that about 200 ml. blood was lost at operation, the third bottle of blood was completed and a third of plasma given. A fourth bottle of blood was transfused after operation.

By 4 hr after operation, when he had recovered from the anaesthetic, he was warm, sweating and thirsty, his blood pressure was 95/65 and his pulse rate 160 His blood pressure soon rose to normal.

At 9 hr after operation, 16 hr after injury, he passed 400 ml. urine (containing blood and granular casts and 1 2 per cent urea), and at 17 hr 90 ml (also with blood and casts, and with 0 3 per cent urea) Since operation he had vomited about 600 ml. and his fluid intake had been about 4½ litres

At 36½ hr after injury he was pale but felt well, his blood pressure was 130/70 His tongue was moist and vomiting had ceased. He had passed only a further 150 ml urine, which had not been examined. By 60½ hr after injury his blood pressure had risen to 165/100 He was listless and drowsy and answered questions only slowly The conjunctivae were slightly icteric, the tongue was moist and clean No more urine had been passed, his blood haemoglobin was 35 per cent and his blood urea 245 mg per 100 ml. Because of the low haemoglobin level he was given three bottles of freshly drawn, cross-matched Group A blood, slowly This did not provoke a transfusion reaction and was followed by the intravenous infusion of ten bottles of glucose saline and 400 ml alkali over 24 hr During this time 300 ml urine was obtained by catheter and contained much amorphous debris, blood and granular casts, the urea concentration was 0 3 per cent His blood pressure remained about 160/100, he became more drowsy and incoherent. He hiccupped frequently but vomited little In the previous 48 hr he had taken about 5 litres of fluid by mouth

There seemed little likelihood of recovery, and the right kidney was decapsulated 94 hr after injury under nitrous oxide, oxygen and ether The kidney felt hard and bulged through the cut capsule

He did not improve after this operation, but became drowsier and more irrational. At 108 hr after injury 24 ml. urine, of the same composition as the last specimen, was withdrawn by catheter He died 4 hr later

Necropsy, 1½ hr after death, revealed no infection of the wounds, there was a large haematoma between the amputation flaps Both lungs were aerated but were wetter than normal, although not grossly oedematous Both kidneys were larger than normal, on section the vascular pattern seemed normal and there was a brownish discoloration of the pyramids The bladder was empty The serous cavities contained a little excess fluid and there was slight excess of cerebro-spinal fluid. The brain was not obviously oedematous

Histological examination revealed small areas of bronchopneumonia The intact and decapsulated kidneys did not differ The glomeruli contained blood Bowman's capsule was not distended but contained remains of red blood cells There was a little eosinophil debris in the proximal convoluted tubules, much golden pigment in the descending loops of Henle and some mitosis in the distal convoluted tubules The collecting tubules were packed with epithelial and red cell casts and the interstitial tissues showed patchy infiltration with eosinophil cells Many fat emboli were found in the lungs, but only a few in the kidney and brain

The histological appearance suggests that the patient died as the result of one or more incompatible blood transfusions *

The next patient was brought to our notice after operation because he had developed renal failure and because he had previously been transfused with blood from the batch which in two other cases provoked an unusual transfusion reaction (see *Case I* 92, pp 35 and 78) Initial blood loss had not been gross and the circulation was maintained, as far as is known, until the final stage The case was not observed completely

**Case I* 67, a soldier aged 25, received several small wounds of the back, both buttocks and legs, the total tissue damage was probably 1–2 hands At the Regimental Aid Post, soon after injury, some bleeding from a wound on the back of the thigh was controlled by a tight bandage He was described as 'shocked + +" and received morphine ¼ gr At 2½ hr after injury at the Ambulance Dressing Station he was described as "cold and shocked', his blood pressure was 120/75 and his pulse rate 80, the pulse 'of fair volume" He was not transfused

At the Casualty Clearing Station, 4 hr after injury, his general condition was good and face colour fair, his extremities were warm, his blood pressure was 110/70 and his pulse rate 100 Before operation he was transfused prophylactically with one bottle of blood This caused severe rigors, the blood was discarded after two thirds of the bottle had been given, and replaced by a bottle of serum

Operation under "Pentothal' anaesthesia (2 5 g) was begun at 7 hr after injury All the wounds were excised and treated with penicillin and dry dressings, and plasters were applied A bottle of blood was transfused The blood loss and the blood pressure at operation are unknown, but the patient s condition did not cause anxiety to the surgeon or anaesthetist

After operation he seemed to do well, his temperature remained 98–99°F (36 7–37 2°C) and his pulse rate about 100 He was given 120,000 units of penicillin intramuscularly daily He did not pass urine, however, till about 50 hr after injury, when he passed about 180 ml containing excess urobilin, protein, a faint trace of haemoglobin and scanty granular casts, but no red blood cells or excess epithelium

When seen by us at 53 hr after injury he was mentally clear, of a good colour and warm, his blood pressure was 130/75, his pulse rate 100 His tongue and skin were dry and he was very thirsty, but vomited what he drank, his haemoglobin was 60 per cent No record of fluid intake or output had been kept, but it was thought that he had been given eight bottles of glucose saline, 4 5 g of both sodium citrate and sodium bicarbonate being added to the first and sixth bottles After this *infusion* he had passed about 350 ml urine, which had not been examined

The urine flow was not maintained Only 90 ml was passed later *in* the day and none subsequently It was dark coloured and contained many brownish granular casts but no red cells, its benzidine reaction was strongly positive

By 120 hr after injury he was dyspnoeic and slightly cyanosed, and the bases of his lungs were dull He received a transfusion of three bottles of fresh, cross-matched blood (Group B) over about 12 hr, and became worse Dyspnoea and cyanosis increased, the jugular veins filled to the ears (he was lying propped up), and slight generalised oedema appeared At 146 hr after injury about 250 ml blood was withdrawn from a vein but produced no improvement He died at 148 hr (the seventh day)

Necropsy 18 hr after death revealed slight general oedema and slight excess fluid in all serous cavities Both lungs were waterlogged, only the anterior margins being completely aerated, there were a few petechial haemorrhages on the surface and small areas of congestion The heart was grossly dilated, especially on the right side, where the auricle and great veins were distended, there was no sign of heart disease The liver was swollen and showed a mottling of pallor and pin point congestion A few submucous haemorrhages were found in the second part of the duodenum The brain was markedly congested and a few petechiae were present in the white matter The only abnormality of the renal tract was slight swelling of the kidneys and some cortical pallor The results of the histological examination are not known except that a moderate degree of fat embolism was found in the lungs ★

WOUND INFECTION

In both series, wound infection developed in a number of patients and caused some deaths

Three of the patients of the Home Series died from gas gangrene, *Case H* 86 and *Case H* 96 at 38 and 39 hr after injury respectively and *Case H* 61 (p 70) on the seventh day Wound infection was also partly responsible for the death of *Case H* 102, 29 hr after injury

Some patients also required further operations because of ischaemic gangrene of the damaged limbs

One, *Case I* 82, soon after operation developed signs of an abdominal complication from which he died on the sixth day Necropsy, 1½ hr after death, revealed a gross, acute, ulcerative and gangrenous gastro-enteritis for which no cause was found The histological appearances indicated that the patient had for a long time been suffering from chronic gastritis

PULMONARY COMPLICATIONS

Pulmonary complications of a varied nature arose in a number of patients, several died

Case I 28, the only example in either series with a wound of the abdominal wall, developed signs of right lower lobar collapse about 50 hr after operation, the collapse was confirmed by X-ray examination There had been no respiratory difficulty at operation, which had been carried out under ethyl chloride followed by endotracheal ether through the Oxford vaporizer, and circulation had been maintained throughout without transfusion The collapse was probably due to restriction of the respiratory excursion by the painful wound of the abdominal wall

Case H 82 who had moderate injuries but much blood loss, and was inadequately transfused until after operation (p 67), displayed signs indicating pulmonary infarctions, probably due to emboli, from the eighth day onwards He was not followed in detail, but a month later the emboli seemed to have ceased and he was transferred to another hospital for convalescence

In two instances bronchopneumonia followed the inhalation of vomit at operation In *Case I* 104 (p 55) lung abscesses also developed, but the patient recovered after a stormy convalescence *Case H* 108 died

Case H 108, a well built lad of 18, received in an air raid multiple large wounds of the left thigh and both legs, with a compound fracture of the left tibia and a perforating wound of the hand the tissue damage was 3–5 hands When he was seen

at 1½ hr after injury his face colour was good and he was not cold, his blood pressure was 120/70 and his pulse rate 94 His haemoglobin was 55 per cent He was given a prophylactic transfusion of one bottle of plasma before operation and a second during it The circulation was maintained

Operation under nitrous oxide, ether and oxygen anaesthesia was begun 3½ hr after injury and lasted 1½ hr Two surgeons operated, the wounds were excised and plasters applied Probably not more than 250 ml blood was lost Early in the course of the operation the patient vomited and inhaled the vomit For the remainder of operation the blood pressure showed a large respiratory variation from 120 to 160, his pulse rate rose to 150

After operation the respiratory variation subsided, his blood pressure coming to a level of about 115/60 Two bottles of blood were transfused The patient remained warm, with a good colour

★By 14 hr after injury his face was flushed and a little cyanosed, his respirations were 40, his blood pressure was 100/35 and his pulse rate 150 Scattered rales were heard over the right chest and there was a large area of dullness at the right base The jugular venous pressure was not raised X-ray examination showed patchy consolidation of the right lung He was drowsy and semi comatose and later became delirious and increasingly restless His axillary temperature rose to 103°F (39 5°C)

By 17 hr after injury crepitus was thought to be detected in the thigh and gas gangrene was suspected He was given one bottle of 5 per cent dextrose and 30,000 units of gas gangrene serum intravenously By 20 hr he was violently restless and had forcibly to be restrained The radial pulse was impalpable, the apex rate 170, the respirations 52, his extremities were warm He was taken to the theatre at 20½ hr and the administration of nitrous oxide and oxygen was begun, but he died 10 min later No evidence of gas gangrene was found

Necropsy, 40 hr after death, revealed no signs of wound infection Both lungs were congested and oedematous, though not grossly, and showed a few surface petechiae, fresh interlobar pleurisy on the right side and areas of early broncho-pneumonia The other organs showed nothing of note A moderate number of fat emboli was found in the lungs but none in the brain or kidneys ★

In a few patients, incompletely observed, the pulmonary complications were possibly due to fat embolism, usually the pulmonary signs were associated with signs of cerebral fat embolism, but in the two cases summarised below these latter were lacking

Case H 110, a man aged 39, received in an air raid bilateral, simple, comminuted fractures of the femora and a compound fracture of the right tibia, with tissue damage of 3–5 hands

At ½ hr after injury he was pale and in great pain, his blood pressure was 115/70 and his pulse rate 76 He was given morphine ¼ gr, put to bed in his clothes with the bed foot raised, given oxygen by mask and warmed by an electric cradle By 1½ hr his blood pressure had fallen to 85/50 and his pulse rate increased to 96 Transfusion of two bottles of plasma in an hour raised his blood pressure to 115/65 and his pulse rate to 112

Operation, under 2 g 'Pentothal', was begun at 2¾ hr after injury and lasted ¾ hr, consisting of excision of the leg wound, application of plaster and extension One bottle of blood was transfused, his blood pressure remained about 115/55 and his pulse rate rose to 140

After operation the circulation was maintained At 22 hr after injury he was fairly comfortable, had passed urine and was not cyanosed, his blood pressure was 120/70 and his pulse rate 112 His respirations were 26 per min

★By 28 hr after injury he was very distressed, sweating, extremely dyspnoeic (respirations 60) and grossly cyanosed, the veins were congested and moist sounds were heard in the chest, his blood pressure was 115/65 and his pulse rate 160 He

was given oxygen by mask and remained in this state for 2–3 hr, after which time he gradually improved By 55 hr after injury he was again fairly comfortable and no longer cyanosed, his blood pressure was 140/80, his pulse rate 92 and his respiration rate 24 The only abnormal signs detected in the chest were a poor air entry at the left base and moist sounds at both bases, he did not at any time produce sputum His further course was uneventful ★

Case H 34, a soldier aged 26, sustained a simple fracture of the right tibia and a minor scalp laceration in an accident, the tissue damage was less than 1 hand He was transported 10 miles to hospital without splinting There, 2½ hr after injury, his face colour was good, his blood pressure 130/80 and his pulse rate 190 He was given morphine ¼ gr, the scalp wound was cleaned and the leg splinted temporarily He remained in good condition

At 34 hr after injury, under a spinal anaesthetic, the fracture was reduced, a plaster applied and the scalp wound sutured under a local anaesthetic He vomited once during operation

★By 42 hr he was dyspnoeic and slightly cyanosed, his mouth temperature was 101°F (38 3°C) and his pulse rate 100 His haemoglobin was 100 per cent and his white blood count 22,000 A patch of bronchial breathing was detected in the right chest Sulphapyridine therapy was started

At 57 hr after injury his fever and tachycardia persisted The dyspnoea had increased and moist rales were heard throughout the chest X ray examination revealed marked increase in density over both lung fields, and many petechial haemorrhages were noted on the anterior surface of the body The optic fundi were normal Fat embolism was suspected

His condition steadily deteriorated, although he remained conscious and rational and without signs of cerebral involvement He died at 100 hr after injury

At necropsy, exploration of the fracture site showed no gross muscle laceration Petechial haemorrhages were present in the skin, pleurae and pericardium Both lungs were voluminous, firm and purple red The cut surface was smooth and oozed very dark blood and yellowish globules, apparently fat Microscopical examination of fresh sections of the lungs stained for fat showed innumerable fat globules of varying sizes ★

CEREBRAL FAT EMBOLISM

Cerebral fat embolism was diagnosed in seven patients Of these five died and were found to have fat emboli in the brain and other parts of the body (p 95) Coma set in more or less rapidly at various times after wounding, 7 hr in two cases, 20–30 hr in four and 65 hr in one, it was preceded or accompanied by mental confusion and drowsiness and sometimes by signs of pulmonary disturbance (e g cyanosis, adventitious signs in the lungs) In two cases the petechiae in the skin were noted to come in crops Neurological signs were scanty and variable, an extensor plantar reflex was noted in three cases, incontinence of urine in two The only focal sign recognised was a transient unilateral paralysis of the face in one case Death occurred between 12 hr and seven days after the onset of coma, in three cases it seemed due to bronchopneumonia

Deaths and Necropsy Findings

INTRODUCTION

Of the 230 patients observed in England and in Italy, 38 are known to have died Data relating to the deaths are given in Tables 16 and 17

TABLE 16

The causes of death and the incidence of fat embolism patients with limb injuries

Patient	Size of wounds	Time after injury	Cause of death	Fat emboli Lungs	Fat emboli Kidneys	Fat emboli Brain
I 105	Very large	3 hr	Haemorrhage	+++	0	
H 94	Moderate	3½				
I 103	Very large	3½		+	+	0
I 100		4 „		+++	+	0
I 107		6 „		++	0	0
H 113		8½	manipulation at operation			
H 111		10½				
H 118		11				
I 4	Small	[illegible]	? Respiratory obstruction due to Pentothal ?			
H 104	Large	13	Haemorrhage manipulation [illegible] operation			
H 112	Very large	13½	pulmonary fat embolism	+++	+++	
H 119		14		++	++	+
I 92	Large	17	transfusion of bad blood	++	0	
I 101	Very large	17		+++	+	+
I 5	Small	17	?	++		
H 101	Large	18 „				
H 97	Moderate	19½	? infected plasma transfusion	++	0	
H 108	Large	20½	Bronchopneumonia anaesthesia	++	0	0
I 106	Very large	21	Haemorrhage	+	0	0
I 87	Large	23		++	+	0
H 103	„	27				
H 102	„	29	Wound infection pulmonary oedema	+	0	0
H 120	Very large	30	Haemorrhage			
H 86	Moderate	38	Gas gangrene			
H 96		39				
I 99	Very large	45	Bronchopneumonia cerebral fat embolism	+++	+++	+++
I 71	Moderate	[illegible]	Haemorrhage cerebral fat embolism bronchopneumonia	+++	++	++
H 107	Large	54	„	+++	+++	+++
H 74	Moderate	62	wound infection			
H 23		5 days	Renal failure			
I 50		5	Bronchopneumonia cerebral fat embolism	+++	+++	++
H 34	Small	5	pulmonary fat embolism	+++		
I 95	Very large	5	Renal failure	+++	+	+
H 116		5		++	++	+
I 82	Large	6	Acute ulcerative and gangrenous gastro-enteritis	+	0	0
I 67	Moderate	7	Renal failure pulmonary oedema	++		
H 61		7 „	Gas gangrene	++	0	
I 59		9	Bronchopneumonia cerebral fat embolism	+++	+++	++

Fat emboli
- 0 None
- \+ Few
- ++ Moderate number
- +++ Many

TABLE 17

Deaths related to tissue damage

Size of wounds	Home Series		Italian Series		Total		
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Percentage mortality
Small	45	1	27	2	72	3	4
Medium	55	7	44	4	99	11	11
Large	10	6	21	3	31	9	29
Very large	10	7	18	8	28	15	54
Total	120	21	110	17	230	38	16.5

All 17 patients of the Italian Series were examined, usually within a few hours, after death; the examination was either witnessed or conducted by us in all but two cases. Histological examination was made in all but one. We are indebted to Professor G. P. Wright of Guy's Hospital for the preparation and examination of the sections. In the Home Series 13 of the 21 cases were examined after death, the examination being witnessed by us in 6 instances; of the remainder the reported details are scanty. Histological examination was made in 9 cases.

It will be seen that only a small proportion of those with minor wounds, but more than half of those with very large wounds died. The method of selecting the cases for the two series exaggerates the mortality in the cases with the smaller wounds, since we were on the look-out for patients with small and moderate wounds whose state departed from the normal, and particularly for those said to be "shocked." Among those with large and very large wounds, on the other hand, the mortality may fairly be taken as representing that to be expected under the prevailing conditions, for we included in the series all such cases coming to our notice. The mortality among those with large and very large wounds is considerably less in the Italian Series than in the Home, although it is still high. The difference may be due in part to the greater age of the Home Series, in which the survivors are on the whole younger (average age 31 years) than those that died (average age 52 years), but we attribute it mainly to the better treatment of the Italian cases and in particular to their more generous transfusion. As is shown in Table 16, the cause of death in most of those with the larger wounds is interpreted as gross blood loss inadequately treated.

Three quarters of the deaths occurred after operation. Only seven patients died before operation was attempted, three died at operation, all of them in the Home Series. Moreover, approximately half of the fatal cases died within 24 hr. of injury, most of them from circulatory failure following gross blood loss. The later deaths were caused mainly by some complication such as infection, fat embolism or renal failure.

In the majority of cases necropsy did little to elucidate the cause of death. Of all the organs the lungs were most frequently abnormal. No significant changes were found in them in nine patients, most of whom died within 12 hr. of injury, but in the remainder they displayed varying degrees of

congestion and oedema, often with petechial or larger haemorrhages and more or less widespread bronchopneumonia in addition The pulmonary oedema was in most instances not gross In only two cases were the lungs waterlogged, in *Case H* 102 this probably resulted from infection and belated excessive transfusion, and in *Case I* 67 from renal failure and terminal transfusion

If it is accepted, as for clinical reasons we think it should be, that the chief cause of death in these cases is inadequately treated gross blood loss, the paucity of gross tissue change is not unexpected With the methods now at our disposal, necropsy can do little more in such cases than confirm that no important injury has been overlooked during life and reveal the presence of unsuspected complicating factors that may have contributed to death (e g fat embolism, infection of lungs, bleeding into a stump) We deal only with the chief complicating factor, namely, fat embolism

FAT EMBOLISM

Table 16 shows that pulmonary fat emboli were demonstrated in all the 25 cases in which the lungs were examined, renal and cerebral fat emboli were found in about half of them* Analysis of the findings provides several points of interest from both the pathological and the clinical aspects

Degree

It is not a simple matter to assess the degree of fat embolism We do it roughly on the appearance of the sections viewed under a 2/3 objective, grouping them according to whether the emboli seen are many, moderate in number, or few

Pulmonary fat emboli were, as we have said, found in all the 25 patients examined, many in 11, in moderate numbers in 10 and few in the remaining 4 In some cases the emboli lay mainly in the smaller vessels (under 30 μ diameter), in others in the larger vessels and in others again in both

Renal fat emboli were found in 13 of 22 patients whose kidneys were examined, many in 5, in moderate number in 3 and few in 5 They were found mainly in the glomerular capillaries, less frequently in the intertubular vessels of the cortex and much less frequently in the medulla

Cerebral fat emboli were found in 9 of 17 patients whose brains were examined, many in 2, in moderate number in 3 and few in 4 They were confined to the minute vessels and more frequent in the grey than in the white matter

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* Histological preparation and examination for fat embolism were carried out by members of the Team We emphasize the need for great care in handling the tissues after death when searching for fat emboli, because fat is liable to escape from the vessels, particularly the larger ones Blocks for microscopic examination should be removed from organs, handled as little as possible and after fixation and washing, embedded in gelatine The frozen sections should be at least 15 μ thick and, during staining and mounting subjected to minimal manipulation and disturbance from diffusion currents Unless these precautions are taken fat embolism is liable to be either missed or underestimated

In most of the cases of both series, sections were prepared in this way from blocks taken one from each lower lung lobe (in a few cases from other lobes also) one from each kidney, one from the brain cortex, usually in the Rolandic area and, in the Italian Series, one from the basal ganglia In a few cases other organs were also examined

The fat stains used were Sudan III and Scarlet Red

Analysis suggests that the occurrence and degree of systemic fat embolism, as exemplified by the brain and kidney, depend in large part on the degree of pulmonary fat embolism Table 18 shows the degree of cerebral fat embolism related to that of the lungs, and a similar relationship was found to

TABLE 18

Relationship between frequencies of pulmonary and cerebral fat emboli

Pulmonary emboli	Cerebral emboli: Many	Moderate	Few	None
Many	2	3	2	1
Moderate	—	—	2	3
Few	—	—	—	4

hold between the kidneys and lungs in general, the more fat there is in the lungs the more there is likely to be in the systemic vessels Other factors, however, probably influence the amount of fat passing into the systemic vessels For example, it may be that fat emboli do not pass rapidly through the lung capillaries (see below) Lack of sufficient time for passage might account for the lack or sparseness of systemic emboli in *Cases I* 105 and *I* 100, whose lungs contained much fat but who died soon after injury, at 2¾ and 4 hr respectively Again, any factor raising the blood pressure in the pulmonary artery or dilating the pulmonary capillaries might be thought to favour the occurrence of systemic embolism It is suggestive from this point of view that *Case I* 80, who had large wounds of the legs and was mentally clear 7 hr after injury, with a blood pressure of 100/70 and a pulse rate of 136, passed into a deep coma during the ¾ hr over which he was transfused with two bottles of blood, during which his blood pressure rose to 145/60 and his pulse rate to 154

The occurrence of skin petechiae in crops during life suggests the intermittent discharge of emboli from the lungs, as does also the occurrence, disappearance and recurrence of mental changes For example *Case I* 61, with large wounds of the legs, was mentally confused 10½ hr after injury, when his blood pressure was 50/30 and his pulse rate 124 Transfusion restored his blood pressure to 110/65, but some mental confusion and amnesia persisted About 12 hr later he seemed well and was considered fit for evacuation, but a few hours later he was in deep coma

Relation to injury Analysis suggests also that the degree of pulmonary embolism depends, at least in part, on the extent of the injury In the 11 patients with very large wounds, the lungs contained much fat in 6, a moderate amount in 3 and little in 2 In the 6 with large injuries, the lungs contained many emboli in 1 only, a moderate number in 3 and a few in 2 Against this it is to be noted that of the 8 patients with moderate and small wounds, many emboli were found in 4, and a moderate number in 4 also It is to be remembered, however, that the cases with large and very large injuries died mainly from the effects of blood loss and are thus unselected

for fat embolism, while the group with small and moderate wounds includes at least four (*Cases H* 34, *I* 50, *I* 59, and *I* 71) in whom fat embolism was probably a factor contributing materially to death, who would thus be expected to show an unusual degree of pulmonary fat embolism

It has long been thought that fractures of the long bones predispose patients to fat embolism, though this is known to occur in the absence of bony fracture Most of our patients had fractures of the long bones, in *Case H* 34, with many pulmonary emboli, the only injury, apart from a minor scalp laceration, was a simple fracture of the tibia But the cases include five who had no bony injury and suffered no section of a bone at operation, the lungs contained many emboli in *Case I* 59, a moderate number in *Cases H* 108, *I* 67 and *I* 5, and a few in *Case I* 82

Speed of Onset

It seems also that the fat may reach the lungs soon after injury, for many emboli were found in *Cases I* 105 and *I* 100, who died approximately 3 and 4 hr respectively after wounding But this is not always so, in *Case I* 103, also with very large wounds and also dying 3½ hr after injury, the lungs contained only a few emboli The blood pressure was low throughout in all these three cases

Further, there seems to be a relationship between the time of death after injury and the distribution of the fat in the lung vessels In general, where the patients died soon after injury the fat was found mainly in the larger branches of the pulmonary artery, while in those dying later it had penetrated to a greater extent into the smaller arterioles and the alveolar capillaries For example, in *Case I* 105, dying 2¾ hr after injury, there was little fat in the vessels with a diameter under about 30 μ, while in the larger vessels many globules lay embedded in blood In *Case I* 99, dying 45 hr after injury, not only the larger vessels but also the capillaries contained much fat In *Case I* 50, dying 102 hr after injury, the fat was sparse in the larger vessels and lay mainly in those of less than about 30 μ in diameter

Size of Emboli

These findings suggest that most of the fat arrives at the lung as particles too large to pass at once into the finer vessels There is support for this suggestion in the fact that in the larger vessels the fat takes the form of globules embedded in blood, which, though ranging in diameter from less than 10 μ up to about 100 μ, are most commonly 30–50 μ in size In the smaller vessels, seen in longitudinal section, the emboli are mainly cylindrical, suggesting that they have been moulded to this shape from spherical globules forced into vessels too narrow to admit them undeformed, while Y-shaped emboli may be seen filling the stem and limbs of a bifurcating vessel In the brain and kidney, on the other hand, the fat is almost confined to vessels of less than 15 μ in diameter, globules are rarely seen embedded in blood in the larger vessels, and such as are seen are seldom over 30 μ in diameter

The size of the fat globules in the larger pulmonary vessels suggests that they may be derived from damaged fat cells at the site of injury Fat cells

commonly measure 30–50 μ in diameter, so that their contents when released might well give rise to fatty globules of this size

Clinical Consequences

Although we have discarded the view that fat embolism, particularly of the central nervous system, is a major factor in the production of "shock" after injury, we remain largely ignorant of the extent to which it may affect the clinical state A serious difficulty is the separation of the effects of fat embolism from those of haemorrhage The grossest degrees of fat embolism are likely to occur in those patients whose wounds are very large, that is, those who suffer much blood loss, and both fat embolism and haemorrhage result in tissue anoxia

Cerebral The coma produced by cerebral fat embolism is generally recognized In these patients it was associated in two cases with many, and in three with a moderate number, of emboli in the brain, but did not occur in the four cases in whom few emboli were found Minor mental disturbances that might be attributed to fat embolism were also noted in a number of other patients after operation, and other signs, such as the temporary partial blindness of *Case I* 98, could be regarded as the expression either of gross blood loss or of fat embolism It is uncertain whether or not embolism of the central nervous system causes hypotension after injury, as, on theoretical grounds, it well might That it usually does not is clear, since in all but two of the seven patients the blood pressure was normal when the signs suggesting cerebral fat embolism appeared and was well maintained until near death In *Case I* 71 (p 69), certainly, it was low at this time and in *Case H* 107 (summarised below) it fell progressively soon afterwards, but both had been too little transfused previously The progressive decline of the blood pressure and death of *Case H* 107 are more probably attributed to further bleeding around the fractured femur, for a gross extravasation of blood was found here at necropsy

Case H 107, a woman aged 31, received large wounds (simple fracture of the left femur, compound fracture of the lower end of the left tibia, a 5 in wound over the right Tendo Achilles and many small cuts and bruises on the body generally) in an air raid, and her left foot was trapped by a beam She was given morphine ¼ gr 1 hr later and was released from the beam after 4½ hr, when a doctor administered open ether and amputated the left foot On the way to hospital she recovered from the anaesthetic and talked, and was admitted to hospital [illegible] hr after injury very shocked

At operation under open ether, about 8 hr after injury, the left leg was amputated below the knee (the fracture of the femur was not noticed) and the wound of the right leg excised Her condition was said to have been very bad, her blood pressure unmeasurable and her pulse impalpable, but transfusion of two bottles of blood improved her greatly

★On recovery from the anaesthetic she talked and was cheerful and comfortable, and her pulse was good During the remainder of the day, her pulse rate remained about 100 and her mouth temperature about 100 F (37 8° C) The next morning, 26 hr after injury, she was wakened by the nurse and said she felt well Half an hour later she was comatose, her pulse rate was 140, the pulse was strong, respirations were 22, and her mouth temperature was 98 4° F (36 9 C) The coma deepened, her respirations became stertorous and their rate rose to 40

At 31 hr after injury she was deeply comatose, her blood pressure was 120/65 and her pulse rate 152, the skin was pale and warm, the forearm veins relaxed, the jugular pressure was not increased, the pupils were small and equal and without reaction to light, the eyes were divergent and moved independently, there were a few petechiae on the chest The fracture of the femur was then recognised The patient remained deeply comatose throughout the day, her pulse rate remained over 140 and her blood pressure fell to 95/60 at 39 hr and 50/35 at 41 hr after injury Cheyne-Stokes respiration was not observed to occur She died 54 hr after injury

Necropsy revealed, in addition to the injuries noted above, a gross extravasation of blood in the fractured thigh, and a small subdural haemorrhage in the left middle fossa at the base The lungs were oedematous, their pleural surface irregular from emphysema and collapse, and showed some petechial haemorrhages, droplets of fat, together with oedema fluid, exuded from their cut surfaces Petechial haemorrhages were seen also in the peritoneum, pericardium, small gut and skin Microscopic examination showed many fat emboli in the brain and spinal cord, lungs, kidneys and other organs No other gross histological abnormalities were detected ★

Renal It is uncertain whether or not renal fat embolism may result in a clinically recognisable disturbance of renal function Of the four patients in whom many emboli were found, two (*Cases I* 99 and *I* 101) died before renal failure could be obvious In the two who survived longer and who presented signs of cerebral fat embolism (*Cases I* 50 and *I* 59) nothing was noticed to suggest renal failure Two patients who died in renal failure were examined for fat emboli in the kidneys, but as only a few were found in one (*Case I* 95) and a moderate number in the other (*Case H* 116) it is unlikely that the degree of fat embolism was sufficient to contribute materially to the renal disturbance

Pulmonary In most of the 11 patients in whom many pulmonary fat emboli were found after death, their presence had been unsuspected during life, and even in retrospect there is nothing to differentiate their course from that of those in whom only a few or a moderate number were later discovered The only unusual features were the cyanosis and respiratory disturbance which were associated with the initial circulatory failure of *Cases H* 112 and *I* 71, the cyanosis which developed later in *Cases I* 80 and *I* 59, who also developed signs of cerebral embolism, and the adventitious sounds heard in the chest of *Case I* 99

It might be thought that blockage of numerous pulmonary vessels would embarrass the circulation, and not only interfere with the oxygenation of the blood but also, perhaps, lead to congestion of the systemic veins and to a fall in the systemic blood pressure But we have seen no evidence to suggest that pulmonary fat embolism produced any of these effects For example, in three of the patients who displayed skin petechiae and signs indicating cerebral fat embolism, and who therefore probably had a gross degree of pulmonary embolism, the jugular venous pressure was not increased and the arterial blood pressure was normal Abundant evidence has already been given that the main cause of persistent low blood pressure is gross blood loss

Diagnosis and Treatment

We have completed the examination of the course of illness following limb injuries and have shown the importance of blood loss as the prime

determining factor We now review the findings for the practical guidance they offer to the clinician

In general the patients with smaller wounds and blood loss, who form the majority of the injured admitted to civilian hospitals, give little trouble in their course towards recovery It is those with the larger wounds or blood loss who become dangerously ill, and what follows applies particularly to these more seriously injured patients who, although less common, are important, since the securing of their recovery taxes to the full the skill of those attending to them

We lay the greatest emphasis on diagnosis and treatment in the initial stage, for if at that time the patient's state is correctly assessed and the proper treatment carried out much of the illness occurring at operation and after should be avoided

BEFORE OPERATION

Diagnosis

It will be clear that the chief objective of diagnosis when the patient is first seen is the assessment of blood loss The most direct and accurate means is by measuring the blood volume, but this is not always practicable The methods so far available are not simple, rapid or foolproof enough for routine clinical use Moreover in the most important cases, those who have lost much blood, venous constriction may make the necessary blood sampling impossible, and the first consideration must be rapid transfusion to save life However, in the *great majority of cases* blood loss can be estimated by other methods with an accuracy sufficient to guide treatment clearly

At the bedside the most valuable index of blood loss is wound size If this is classified as already described, then in general it may be concluded that (*a*) with small wounds (less than 1 hand in volume) little blood has been lost, rarely more than 20 per cent and commonly less than 10 per cent of the total blood, (*b*) with large wounds (3–5 hands) blood loss has been of the order of 40 per cent, (*c*) with very large wounds (5 hands and over) it has been of the order of 50 per cent Moderate sized wounds (1 and under 3 hands) offer less clear indications, the blood loss may have been much or little, though usually between 20 and 40 per cent

No matter how trivial the injury may seem at first sight, the patient should be undressed and examined, nothing is to be gained and much may be lost by delay, and it is only in the most serious cases that thorough examination of the wounds and the state of the circulation should be delayed because of the urgent need to arrest haemorrhage or to give immediate transfusion

The second valuable index of blood loss at the bedside is the level of the systolic blood pressure, for this shows how far blood loss has reduced the blood volume In general it may be concluded that (*a*) if the blood pressure is at least 100 mm Hg, the blood volume remains above the critical level of 70 per cent normal, (*b*) if it is over 140, the blood volume is at least 80 per cent normal, (*c*) if it is below 100, the blood volume is below 70 per cent normal

These two indices alone usually leave little doubt about the order of the blood loss and the blood volume, and their evidence is usually concordant

Small and moderate wounds are usually associated with normal blood pressures, a combination which makes it reasonably certain that blood loss has been insufficient to reduce the blood volume below the critical level, if they are associated with hypertension the blood volume is probably 80 per cent or more Large wounds are usually, and very large wounds almost always, associated with low blood pressure, and the combination indicates a blood volume below 70 per cent normal, the larger the wounds the further below this level the blood volume is likely to be The unusual combination of large or very large wounds and a normal blood pressure *indicates that less blood* has been lost than is usual from such wounds but that the blood volume, although it remains above the critical level, is probably not far above it The other unusual combination, of a low blood pressure with small wounds, is of doubtful interpretation, on occasion much blood can be lost from small wounds, while on the other hand blood pressure may be lowered by a faint (vasovagal syndrome)

While wound size and blood pressure provide the main elements for diagnosis, this may be refined by the evidence from other subsidiary features

Indications of blood loss may be available in the amount of blood shed on to the dressings and clothes, information may be obtained from the patient himself, his attendants and the witnesses of his injury But it is emphasised that, while positive evidence of this nature may be of value, its absence cannot be taken as evidence against blood loss, for, although those giving first aid to the wounded should be trained to observe and record evidence of the amount of blood lost, they cannot always be relied on to do so

Further indications of the level of the blood volume are provided by pulse rate, face colour and temperature of the extremities Each of these by itself is of little value, but their combinations with each other and with the blood pressure provide circulatory patterns of diagnostic importance Thus a low blood pressure combined with a fast pulse rate, pale face and cold extremities is a clear indication of blood loss sufficient to reduce the blood volume below the critical level, even though the wounds are small The pattern of a very low blood pressure (under 70 mm Hg), impalpable pulses, very rapid heart rate and marked pallor, often with the addition of great restlessness and dyspnoea, clearly indicates great blood loss and a blood volume reduced to the point of death, to 60 or 50 per cent normal or less

On the other hand the combination of low blood pressure with pallor, cold extremities and a slow pulse rate indicates a circulatory depression brought about by sensory and emotional stimuli rather than by blood loss, even when sighing respirations, sweating, nausea and vomiting are also present This combination does not exclude severe loss of blood, which however is unlikely if the wounds are small or if the blood pressure recovers quickly when the patient is placed in the supine and head-down position

Where the blood pressure is normal the associated signs may also be of use, in determining whether the blood volume is nearer the normal than the critical level Thus a good facial colour, a normal pulse rate, and warm extremities indicate that in all probability the blood volume is nearly normal,

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while a pale face, a fast pulse and cold extremities indicate that the blood volume is probably between 70 and 80 per cent normal

In interpreting these circulatory patterns three general points should be borne in mind The first is that the sooner after injury the patient is seen, the more likely are nervous factors to disturb the circulation and to complicate the assessment of blood loss Secondly it is to be remembered that older subjects have on the whole slower pulse rates than younger, and may suffer from a pre-existing hypertension Thirdly, these rules apply in their entirety only to untransfused patients, the modifications introduced by prior transfusion will be discussed shortly

These rules provide a sound basis for foretelling what will happen to the patient and for indicating treatment For example, at the one extreme patients with small wounds and the normal circulatory pattern have blood volumes not far below normal, without transfusion they will maintain their circulation before, during and after operation At the other extreme patients with very large wounds and marked circulatory failure have blood volumes well below the critical level, they are in a dangerous state, and unless they are at once transfused adequately some will soon die, few will long survive operation and the survivors are likely to have a stormy passage towards recovery Between these extremes are patients with moderate or large wounds who maintain their circulation precariously till operation, but who, unless adequately transfused beforehand, are then likely to develop circulatory failure

Usefulness of Individual Signs

Face colour The relegation of facial colour to a secondary place in diagnosis departs from common usage It is fair to say that medical officers in general are greatly influenced in their assessment by facial colour, a man with a good colour is thought to be "all right" and a pale man "in poor condition", "ill", or usually "shocked", often without reference to the level of blood pressure Pallor is commonly taken as an indication for transfusion, even though the blood pressure is normal In discussion, few would admit that their diagnosis of "shock" rested merely on an appreciation of facial colour, but in numerous instances this conclusion is unavoidable For example, we have been called to see a patient because he was said to be "severely shocked" and have found small wounds and normal blood pressure and pulse rate, but a pale face The records accompanying the patients to hospital in Italy not infrequently contained the note that at a certain time the patient was "cold and shocked" and sometimes added the valuable information that the blood pressure was for example, 110/75, and the pulse rate 70 We have on occasion, when examining a patient with a surgeon, asked him whether or not he thought the patient "shocked", his answer was given after a glance at the patient's face In the following instance it is difficult to find any interpretation of the words "very shocked" other than "very pale"

An air gunner, aged 22, returning from a raid, was thrown clear from a crashing bomber He was quickly picked up and taken to sick quarters

Half an hour after injury he was lying in his flying kit under an electric cradle His face was very pale and sweating, his hands were warm, his pulse rate was 110 and his pulse volume good He was mentally a little dazed and was probably concussed, but he was not apathetic, answered questions rationally and knew where he was He was thirsty He complained of pain in the right lower chest and his respirations were *grunting There were small abrasions of the face He was given morphine* ¼ gr and watched

At 1¼ hr after injury his clothes were cut off, and no gross injuries were found anywhere He was still pale, warm and sweating, with a blood pressure of 110/70 and a pulse rate of 92 He soon fell asleep

At 2 hr he was less pale, fairly comfortable and drowsy, his blood pressure was 110/70 and his pulse rate 88 The observer accompanied him to hospital in the ambulance

★On admission 3½ hr after injury he was still pale and warm but not sweating, his blood pressure was 135/75 and his pulse rate 110 He passed 20 oz urine Examination revealed no injuries beyond bruises and abrasions and signs of a small right-sided pneumothorax (which, with a fracture of the tenth right rib, was later found by X ray) The medical officer was informed of the earlier findings He considered *the patient very shocked* and so described him in the hospital records, ordering warmth, morphine ¼ gr and transfusion of one bottle of blood and one of serum

At 4½ hr, during blood transfusion, the patient was comfortable, less pale, warm and drowsy his blood pressure was 135/80 and his pulse rate 110

A few hours later he was reported to be 'in good general condition' His further course was uneventful ★

While it is true that those who have lost much blood and whose blood volume is below the critical level are all, or almost all, pale, yet pallor is not uncommon soon after injury among those whose blood loss is negligible It is true that one can distinguish a pallor that persists, which is more likely to indicate blood loss, from a pallor that soon passes, but this point is not of much practical value, since it is important that blood loss should be recognized and treated without delay It should also be remembered that, although with a selected group of patients like fit young soldiers it is fair to assume that facial colour was good before injury, the same assumption cannot be made for civilian patients

On the other hand, some patients were seen, particularly after operation, whose blood pressure was low, but who were not pale, they were regarded by the surgeon as "not shocked" and "all right"

There is, moreover, no objective measure of facial colour, its appreciation is much affected by the light in which it is observed, it may be obscured by grime, pallor may be enhanced by smears of blood on the face It is clear, *therefore, that in the initial stage pallor is useful only* as a warning sign that much blood may have been lost, and that other and more certain signs should be looked for

Hypertension The significance here attached to hypertension differs from that usually accepted Hypertension is often regarded as an indication of "impending shock" The evidence for this is not clear, but the view seems to arise from a belief that after haemorrhage the blood pressure is maintained for a time by a "compensatory" vasoconstriction, and a rise of the blood pressure above normal indicates an "over-compensation" which is likely soon to give way The evidence discussed earlier shows that hypertension

in untransfused cases is generally associated with a small blood loss, that it arises probably from emotional or sensory stimuli and that it is of good prognostic import

Pulse pressure It is sometimes held that, when the systolic blood pressure is normal, collapse of the circulation can be foretold by a lessened pulse pressure caused by a rise of diastolic pressure, but the evidence of these cases is against this view

There is in the Home Series a group of 12 patients, all with systolic blood pressures of 100–140 and all assessed as losing less than 20 per cent of their blood seven had moderate and five had small wounds None showed a later fall of blood pressure and none were transfused Their diastolic pressures averaged 73 (range 58–92) and their pulse pressures 52 (range 40–70) To compare with this there is a second group of 12 patients, all again with systolic blood pressures of 100–140, but all assessed as losing more than 20 per cent of their blood, all but one had moderate and the remaining one had large wounds In all the blood pressure later fell below 100 and all required transfusion for their recovery Their diastolic pressures averaged 71 (range 60–80) and their pulse pressures 40 (range 25–58) Though pulse pressure in this group is on the whole lower than in the first, the lowering is due not to a raising of diastolic pressure but to a lowering of the systolic, which averaged 125 (range 106–140) in the first and 110 (range 100–130) in the second The average ages of the two groups were 34 and 35 respectively

Similarly in the Italian Series there is a group of nine patients with normal blood pressures, all with blood volumes above 90 per cent of the predicted normal Only two showed a later small fall of blood pressure below 100 and one was transfused Their diastolic blood pressures averaged 81 (range 70–100) and their pulse pressures 46 (range 22–60), the systolic pressures averaged 128 (110–140) There is also a group of nine patients with initially normal blood pressures but blood volumes of 67–75 per cent, in seven the blood pressure later fell below 100 and all were transfused Diastolic blood pressures averaged 71 (50–85) pulse pressures 47 (25–70) and systolic pressures 118 (100–140) That is, pulse pressure is the same in both the groups, although the systolic and the diastolic blood pressures are on the whole lower in the second than in the first

It seems therefore, that neither diastolic nor pulse pressure is of value for recognising the degree of blood loss nor for foretelling later circulatory collapse

Treatment

In the early days of the war, the usual treatment given in England to "shocked" cases was rest, often in the head-down position, morphine (usually ¼ gr) and warmth Warming the patient not uncommonly meant heating him under an electric cradle or surrounding him with hot water bottles until he was uncomfortably hot, restless and sweating profusely Rest sometimes entailed leaving him clothed and almost unexamined until he had recovered from his "shock", operation was usually delayed till then even at the risk of the development of wound infection It was thought harmful to operate upon, or even to examine and so disturb, a severely "shocked" patient In addition to these measures, oxygen was often administered and sometimes also such drugs as "Coramine" or adrenaline Occasionally, when leg injuries were present, spinal anaesthesia was induced to relieve "shock" Often transfusion was resorted to only after these other measures

had failed, and was then given slowly and in small amounts It was seldom used prophylactically Early transfusion was regarded by some as dangerous because of the likelihood of renewing bleeding before the surgeon was ready to deal with it, while rapid or large transfusions were thought likely to overburden the circulation, dilate the heart and cause pulmonary oedema Transfusion reactions were common and feared as harmful It was thought useless to attempt the restoration of a "moribund" patient

Looking back from the vantage point of present knowledge, we can see that treatment in those early days was often misdirected and even harmful, avoidable illness and loss of life were the result Later, as shown by the Italian Series, treatment improved Wounds were examined and treated early, undue warming was rare and, most important, transfusion was given earlier and more freely

The experience of the war years clearly answers those practical questions to which, at the beginning of our work, we could find no satisfactory solution, either from published writings or from our more experienced colleagues These questions were "which patients should be transfused, what transfusion fluid should be given, when, at what rate and how much, and when should operation be undertaken?"

Patients to be Transfused

Those patients do best, before, during and after operation, whose blood volume is maintained well above the critical level of 70 per cent normal Hence all patients whose wounds and circulatory state make it likely that the blood volume is below or not far above this level should be transfused, if in doubt, transfuse

Fluid to be Transfused

Since loss of whole blood is the chief factor causing circulatory disturbance, blood is the best fluid to transfuse, provided its quality can be relied on In civilian practice there should be no question about this, but on active service, where conditions for preparation, storage and transport may be unfavourable, doubts may arise There was a period in Italy when the quality of the available blood was suspected, but even then there was evidence of mismatched transfusion in only one case and suspicion in one other in two other cases it was suspected that blood abnormal in some other way had been transfused

Circumstances arise, not only on active service but also in ordinary practice, where blood is not available for transfusion However, the blood volume can be raised and the blood pressure restored by plasma or serum alone, even after gross loss of blood In such cases the patient remains seriously deficient of red cells, e g *Case I 53*, who had lost about 60 per cent of his blood, had after the transfusion of four bottles of serum a measured blood volume of 77 per cent normal, but his red cell volume was only 35 per cent normal Too few cases have been treated with plasma or serum alone to show whether or not their subsequent course is less satisfactory than when blood is used It is probable, however, that a patient with a low red cell volume is less able to supply oxygen to his tissues, to carry out repair and to prevent or overcome

infection of his injuries than one well supplied in this respect We do not know, however, the level to which haemoglobin may fall without interfering with recovery We prefer that haemoglobin should remain above 60 per cent (9 6 g per 100 ml) and that in any case it should not be allowed to fall below 50 per cent (8 g per 100 ml) for more than a short time

Time of Transfusion

The Home Series shows that in many cases of hypotension the circulation can be restored even though transfusion is delayed for an hour or two On the other hand, the evidence recounted earlier shows that to delay transfusion is bad practice and emphasises two points (i) if a patient with hypotension and injury to limb or soft tissue does not recover promptly when placed in the head-down position, it is unwise to delay transfusion, (ii) if a patient shows a marked degree of circulatory collapse (blood pressure under 70 mm Hg, usually a very rapid heart rate, together with great pallor, cold extremities and often great restlessness and dyspnoea) there must be no delay in beginning transfusion if life is to be saved

One reason sometimes advanced for delaying transfusion was that, if the patient had lost blood, it was better that he should replace it naturally, by passing fluid from his tissues into his vessels, than that he be given an artificial fluid It was thought that if he were well supplied with water to drink he would soon replace the deficient fluid But in man the addition of fluid after haemorrhage is slow and the blood pressure is not soon restored Estimations of the rate of dilution will be found in Part IV

Rate of Transfusion

Slow transfusion not only delays recovery but, in patients with marked circulatory failure, may result in early death In such cases, therefore, transfusion must be at the rate of a bottle over 5–15 minutes, that is to say, as fast as the fluid will enter the vein under gravity, air pressure or two-way syringe Where, in spite of pressure, the rate of transfusion is slowed by venous constriction, it can be speeded up by applying a hot water bottle over the site of transfusion To give enough blood in as little time as this, it may be necessary to transfuse through two veins Transfusion is usually faster by way of the arm veins than by the leg, and the jugular veins may on occasion offer a better site than either It is not usually necessary to cut down on a vein, for a needle can almost always be inserted by the expert, but if cutting down is necessary there must be no delay

When the patient has responded well to transfusion, its rate should be slowed to a bottle over 1 hr or longer In less serious cases and where transfusion is given prophylactically, the slower rate is sufficient from the first, provided the patient receives an adequate amount before proceeding to operation

Two reasons are often advanced against rapid transfusion, (i) the production of rigors, and (ii) the renewal of haemorrhage

(i) Rigors are more likely to be provoked and to be severe with rapid than with slow transfusion However, there is no evidence that even severe reactions in these patients cause permanent ill effects The chief danger of a

transfusion reaction in dangerously ill patients seems to be that it may cause such a degree of venous constriction as to make it difficult to pump blood in fast enough or to replace transfusion needles and cannulae displaced by the restless patient

(ii) Renewed bleeding was observed in four patients of the Italian Series, all of whom were transfused at the rate of one bottle over 5–10 min It was not avoided by slower transfusion, however, for it occurred also in four patients of the Home Series in whom transfusion was at the rate of one bottle over ½–1 hr The answer to the danger of renewed bleeding is to bear its possibility in mind and to have the means of arresting bleeding at hand In seriously ill patients, the dangers of delayed or slow transfusion far outweigh those arising from the renewal of bleeding

Another danger arises when, to increase the rate of transfusion, air pressure is raised within the bottle, since there is then the possibility of air being forced into the vein as the bottle empties If, however, the patient is carefully attended, as he should be, and the possibility borne in mind, the likelihood of this accident occurring is very small In fact, in the course of these observations we met with only one instance of fatal air embolism from this cause, which happened when the circumstances made close attention by the orderly concerned difficult

Amount of Transfusion

In the early days of the war it was thought that the restoration of blood pressure to 100 mm Hg or over, and its maintainance there when transfusion was stopped or slowed, indicated that an adequate amount had been given It became increasingly clear, however, that this index was unsatisfactory for, although the blood pressure might be maintained while the patient rested quietly in bed, yet circulatory collapse often recurred at operation, even though little more blood was lost The knowledge later gained of the relation between blood pressure and blood volume shows why this was so and why patients then thought to be over-transfused did better than others Restoration of the blood pressure does not mean that the blood volume has been restored to normal, but usually only that it has been raised to the critical level or above, how far above is uncertain In some instances a severe transfusion reaction may raise blood pressure temporarily to normal or above even if the blood volume remains below the critical level At operation, the various factors tending to depress the circulation are the more liable to provoke a sustained and dangerous collapse the nearer the patient's blood volume is to the critical level

The other circulatory features of pulse rate, face colour and extremity temperature do not, in general, help to determine whether or not transfusion has been adequate If, however, transfusion not only raises the blood pressure to normal or above but also slows the pulse rate and replaces vasoconstriction by vasodilatation then blood volume has probably been raised well above the critical level Transfusion seldom results in the restoration of this, the normal circulatory pattern Often, because of the pharmacological properties of the transfused fluids, tachycardia, with or without

vasoconstriction, persists, even though the blood volume is raised to not far short of normal

The most generally useful rule is to restore the blood pressure to normal levels or above, *indicating that the blood volume has probably* been restored to about 70 per cent normal, and to continue transfusion beyond this point with a further amount depending on the level of blood volume it is desired to reach

Whether it is advisable to transfuse enough to restore the blood volume to normal is unknown, for it has not been done in practice Moreover it might be said that, since patients can pass through operation safely with a blood volume lower than normal (about 80 per cent normal) and since there is some risk* attached to the transfusion of stored blood and its products, it would seem advisable to transfuse as little as is compatible with safety during operation Allowing a margin for renewed bleeding at operation and for continued oozing afterwards, 90 per cent normal seems a safe level of blood volume to aim at for the beginning of operation, that is to say, after the blood pressure has been restored, the patient should be given a further transfusion equivalent to 20 per cent of his predicted normal blood volume

It has been seen that (i) estimation of wound size and examination of the circulatory state before transfusion provide an index to the level of the blood volume and (ii) a bottle of plasma, blood or serum as supplied in England and in Italy may be expected to raise the blood volume by approximately 5, 8 or 9 per cent respectively of the predicted normal blood volume of the average man These data, therefore, provide a useful indication of the amounts of transfusion to be given

1 *a* With an initial blood volume of 60 per cent normal, between one and two bottles of blood or serum or two bottles of plasma should be required to raise blood volume to 70 per cent normal and restore the blood pressure to 100 or more

b With an initial blood volume of 50 per cent normal, between two and three bottles of blood or serum or four bottles of plasma should be needed

c With an initial blood volume of 40 per cent normal, four bottles of blood, three or four bottles of serum or six bottles of plasma should be needed

2 When this has been done, a further two or three bottles of blood or four bottles of plasma should be required to raise the blood volume to 90 per cent normal

For the majority of patients who require transfusion, these data provide a satisfactory indication of the amounts to be given For others, however, particularly those with very large wounds, larger amounts are required To raise the blood pressure to 100 or more, *Cases I* 98 and *I* 106, both with very large wounds and initial blood volume of about 60 per cent normal, required amounts equivalent to 21 and 26 per cent respectively of their

* There is a risk probably low, from mismatched or infected blood and a greater risk of transfusing the virus of serum jaundice from which the mortality is considerable

predicted normal blood volume In *Case I* 110, with very large wounds and initial blood volume of about 50 per cent, the amount required was 32 per cent The reason for these large amounts is unknown, but it is probable that further bleeding was in part responsible

Time of Operation

Patients with small or moderate wounds who have not lost much blood do not need operation urgently, but to prevent the development of infection it is advisable to operate within 6 hr of injury In other cases operation should be undertaken as soon as possible after the circulation is restored If transfusion is carried out properly most patients should be well resuscitated within an hour or two of admission In cases with large or very large wounds it may be necessary to operate even though, because of bleeding or failure of proper response to transfusion, the blood pressure is not restored Nothing is to be gained and much may be lost by delaying operation on such patients Our general experience both in England and in Italy is that there is a period of a few hours after injury when most patients with large and very large wounds can be much improved by transfusion and that the best chance of survival is offered by operating within that period, even though the blood pressure is low The best results were obtained by early operation following early, rapid and adequate transfusion

Other Therapeutic Measures

These are important adjuncts to transfusion Though it may seem that some well known and elementary points are stressed, in practice we found them often neglected

Arrest of haemorrhage It is important not only to replace lost blood, but also to prevent unnecessary further loss In the interval between admission and operation watch must be kept for continued or renewed bleeding, whether or not transfusion is given, and the means of staunching blood must be at hand It is to be remembered that where blood volume is near the critical level a small further loss of blood may be sufficient to reduce it below that level and so precipitate a fall of blood pressure

The head-down position is a valuable measure where there is initial hypotension and where the blood pressure later falls again steeply, and will usually result in raising a low blood pressure by 5–10 mm Hg In instances of the vasovagal reaction it may be enough to restore the blood pressure rapidly to normal It is uncomfortable, however, and should not be maintained longer than is necessary A renewed and sustained fall of blood pressure when the patient is returned to the horizontal is an indication of inadequate transfusion

Morphine should be given to relieve pain and apprehension It is to be remembered that in the presence of gross vasoconstriction morphine given subcutaneously may not be absorbed quickly and further injections may result in an overdose when the vessels are later relaxed Intravenous injection may be substituted and may be required for the speedy relief of severe pain

We have not found the administration of *oxygen*, of "*Coramine*", or of *vasoconstrictor drugs* such as *adrenaline* of value in these cases

Warmth should not be applied as a routine, but only when the patient is cold, and must then be regulated to his comfort Over-warming increases the patient's discomfort and restlessness and may lead to a fall of blood pressure

Rest is important Because of the possibility of originating depressor reflexes, the injured parts must be handled with the greatest care The clothes of the badly injured patient should be cut off Once in bed and examined, the patient should be helped to rest and his wants attended to or, better, anticipated A point often neglected is that as far as possible his anxieties should be allayed, bearing in mind that he is probably in hospital for the first time and may be alarmed by what is done to him and by what he sees and hears unless some kindly explanation is given Particularly in civilian hospitals, patients have complained of the lack of this reassuring attention

Fluids by mouth In the early days of the war it was usual to allow and to encourage the taking of unlimited fluids by mouth The wisdom of this is doubtful, because of the possibility of provoking vomiting at operation It is preferable to give only repeated sips of water even to the avidly thirsty

AT OPERATION

Provided that the loss of blood has been made good beforehand, little difficulty should be experienced at operation Adequately transfused patients, even with very large injuries, can pass through a long and difficult operation without developing circulatory failure then or later

Because of the difficulties that may arise and because of the danger of renewed bleeding, transfusion should be continued slowly as a precautionary measure, so that it may be speeded if required It is simpler and safer to do this than to begin or restart transfusion at operation

The best guide to the patient's state during operation is again the level of the systolic blood pressure A fall of blood pressure due to haemorrhage requires rapid transfusion A steep fall following manipulation indicates that transfusion should be speeded, operation should be suspended until the depression passes, and the head-down position may aid in the recovery It is important to follow the course of the blood pressure after the withdrawal of the anaesthetic at the end of operation, for then it may fall rapidly to dangerous levels If this happens, rapid transfusion is again required

The data do not provide sufficient evidence with which to compare the effects of a long operation with those of a short one It is thought, however, that the manner in which operation is carried out is more important than its length A short operation with rough surgery and inadequate haemostasis may do more harm than a much longer one in which the injured parts are handled as gently as possible and haemorrhage is kept minimal It seems advisable to keep the total length of operation within one hour In cases of extensive and bilateral injuries, two surgeons should operate

The data are not sufficient to allow us to express a preference for any anaesthetic Both in England and in Italy, anaesthetists preferred to use ether and oxygen or a mixture of nitrous oxide, ether and oxygen for the most serious cases, and both seemed satisfactory provided they were skilfully administered

AFTER OPERATION

In the early part of the war, the general opinion seemed to be that a period of hypotension after operation was not of great importance, particularly if the patient was otherwise in "good condition" (which apparently meant "not pale"), and that if he were left in peace, as he ought to be, he would recover satisfactorily As a result opposition was encountered from time to time from both medical and nursing staffs, who felt that continued observation and transfusion of the patient interfered with his recovery It seemed to be thought, even in the cases with the larger wounds, that hypotension recurring in a patient previously resuscitated by transfusion could hardly be due to shortage of blood, unless the loss of blood at operation was gross, and that further transfusion would be likely to overload the circulation and cause death from pulmonary oedema

But the early post-operation period, particularly in those with large and very large wounds which have bled much, is a period of danger, and patients require as much careful attention and skilful handling then as in the periods before and during operation We emphasise that all patients with very large wounds need watching with the greatest care for the first 12 hr after operation, since their life often seems to hang by a thread

In this period the best guide to the blood volume is again the blood pressure, though its indications are less certain than in the initial stage Face colour, pulse rate and extremity temperature give little help

A normal blood pressure again usually indicates a blood volume not below the critical level of 70 per cent normal, the further course is usually uneventful and further transfusion is not required Nevertheless a normal blood pressure occasionally gives a false impression of the circulatory state, and unless the patient is watched he may develop a serious and unnoticed hypotension

A persistently low blood pressure usually indicates a blood volume about or below 70 per cent normal, but occasionally, particularly in patients with very large wounds, it is associated with a blood volume of 80 per cent normal or more, such cases show evidence of good blood flow through their extremities, and the face may be well coloured or pale Such a persistently low pressure indicates the need for further transfusion, which should be continued till the blood pressure is restored

The majority of patients displaying hypotension give rise to little difficulty and the blood pressure should be restored within an hour or two of operation But cases with very large injuries, that is, with tissue damage of five hands or more in volume, may give rise to much doubt whether or not to continue transfusion and how much transfusion should be given Cases

TABLE 19

Summary of transfusion data for six cases with very large limb injuries

(Blood volumes and amounts of haemorrhage and transfusion stated as per cent of predicted normal blood volume)

Patient	Before operation		At operation		After operation									Page reference
					Before blood volume estimation		*Totals from previous columns*		Blood volume estimation			Transfusion after blood volume estimation	*Subsequent course*	
	Transfusion	Haemorrhage during transfusion	Transfusion	Haemorrhage during transfusion	Transfusion	Haemorrhage	*Transfusion*	*Haemorrhage*	Time after operation (hr)	Blood pressure etc	Blood volume			
I 96	33	—	12	5	Nil	—	*45* (B 2S)	*About 5*	3	75/55 Pulse rate 111 Vasoconstriction	71	20 (2B)	Blood pressure restored good progress	76
I 101	17	Little	21	Very little	3	—	*41* (3B 4I)	*Little*	[illegible]	65/10 *Pulse rate* 160 Vasoconstriction	63	[illegible]9 (4B after delay)	*Died from circulatory failure* Result of blood volume not known in time to guide treatment transfusion too long delayed	72
I 104	20	Little seen	20	6	2	Little *seen*	*42* (4B) (? 1P)	*6*	1½	110/60 Pulse rate 120 No vasoconstriction	12[illegible]	Nil	Blood pressure maintained stormy later course pneumonia ; lung abscess	55
I 106	35	Little	16	10	14	Some	*65* (6B 1S 1P)	*About 10*	4	90/30 Pulse rate 108	[illegible]	Nil	Not watched became unconscious and died	75
I 109	*52*	*? Much*	*5*	*? Much*	8	*Moderate*	*65* (5B 6P)	*Much*	4	100/55 Pulse rate 132 Hot *restless*	66	7 (1B slowly)	Blood pressure restored slow recovery wounds became infected	79
I 110	[illegible]	? Much	15	? Much	16	Little	*69* (9B 1½ S)	*Much*	3½	95/60 Pulse rate 152	74	[illegible]4 ([illegible]B 1½ S)	Blood pressure restored *remarkably good* [illegible] *ponse*	33 and 73

B = bottles of blood S = bottles of serum P = bottles of plasma

illustrating this have been described in the preceding pages, the relevant data for six cases are summarised in Table 19 Low blood pressures may not mean that blood volume is below 70 per cent normal (*Cases I* 96 and *I* 110) and it may be well above (*Case I* 106) Though normal blood pressure indicates that blood volume is probably about or above 70 per cent normal, there is no clinical means of determining whether it is near to or well above this level (*Cases I* 104 and *I* 109) Since it is very important that the blood volumes of such patients should be raised well above this level, because of their damaged or unstable circulatory control and because they may bleed further from their wounds for some time after operation, and since they may have already been given so much transfusion that further transfusion is feared as excessive (*Cases I* 106, *I* 109 and *I* 110), it is essential for the proper control of their treatment that the blood volume be measured at this stage Before operation the measurement of blood volume is usually impracticable, but after operation it can usually be done readily, since there is no urgent need for immediate rapid transfusion, and vasoconstriction, if present, is usually not so great as to impede the injection of dye or prevent the withdrawal of blood samples *Cases I* 101 and *I* 110 illustrate well the value of measuring the blood volume after operation In both it had been thought that the transfusion already given was more than enough to compensate for blood loss and it seemed unwise to continue In *Case I* 101, who had been given three bottles of blood and four of plasma, the result of the blood volume measurement (63 per cent) was not known for several hours, and meanwhile only a little glucose saline was given The blood pressure continued to fall, a belated attempt was made to restore it, using four bottles of blood, but it failed and the patient soon died In *Case I* 110, who had already been given nine bottles of blood and rather more than one of serum, the result of the blood volume measurement (74 per cent) was known quickly, and gave us confidence to continue transfusion with two more bottles of blood and one and a third of serum The patient recovered rapidly

In the later post-operation period further transfusion may be required to correct a secondary anaemia For this purpose fresh blood is to be preferred to stored, but it must be remembered that it may be difficult to find a blood suitable for transfusion

Watch must be kept during this period, particularly in those with large and very large wounds, on the fluid intake and output, and for any signs that might indicate the development of complications, especially renal disturbance, fat embolism and wound infection Provided transfusion has been properly carried out, urine flow should be re-established within 24 hr of operation

PART II

INJURIES TO THE ABDOMEN

Introduction

THE work on injuries to the abdomen was not carried as far as that on limb wounds We had had little experience of such cases before going to Italy, and there they were a secondary interest In the first place we studied only the early course of such injuries, and not until almost the end of our work did we attempt a close study of the later stages

The general result of the observations is to show three things first, that before, during and shortly after operation the chief and dangerous illness is circulatory in origin and is due to blood loss from haemorrhage, second, that after operation infection is the most important single factor causing illness and death, circulation being well maintained unless death is imminent, third, that the course after operation is liable to be complicated by disturbances of the fluid and salt balance arising from treatment by gastric suction and the intravenous administration of saline fluids

The Patients, Their Injuries and Blood Loss

PATIENTS

A series of 80 patients was studied at the same hospitals as those with injuries to the limbs, all except one by members of the team Since injuries to the abdomen were much fewer than those to the limbs, the series includes the large majority of all such cases admitted to the hospitals at which we worked The criteria of selection were (a) that the surface wounds or other signs pointed to the possible injury of the contents of the abdomen or pelvis and (b) that the cases were uncomplicated by head injuries or gross injuries to the limbs or chest

The patients were nearly all fit young men, mostly our own troops Eleven were prisoners of war, three were Italian peasants (one a woman) and three were dark skinned Indian soldiers Their ages, shown in Table 20, ranged from 18 to 43 years The great majority were in the twenties or thirties, the average being 26 years

TABLE 20

Ages of patients with injuries to the abdomen

Age	10–19	20–29	30–39	40–49
Number	6	50	21	3

INJURIES

The injuries, like those to the limbs, were caused by weapons of war, only one was due to accident The visceral lesions as revealed by operation

TABLE 21

The visceral injuries in 80 cases

Injuries to Stomach or Intestine	Other visceral injuries						Totals	Serial numbers of cases
	None	(a) Liver	(b) Spleen	(c) Kidney	(d) Bladder and ureters	Combinations of (a) to (d)		
No intraperitoneal perforation								
No intestinal lesion	4*	4 (1C)	2 (2C)	3	—	3 (1G)	16	*B* 1–16
Bruising of intestine only	2 (1C)	—	—	—	1	—	3	*B* 17–19
Extraperitoneal perforation (large intestine)	7	—	—	—	—	—	7	*B* 20–26
Intraperitoneal perforation								
(1) Stomach	2	1	1 (1C)	—	—	2 (1C and P)	6	*B* 27–32
(2) Small intestine	16 (2C 6P)	—	—	—	3 (1P)	1	20	*B* 33–52
(3) Large intestine	7 (3P)	4 (2C)	—	1	—	1 (1C)	13	*B* 53–65
(4) Combinations of (1) to (3)	11 (1C, 1P)	3	—	1 (1C)	—	—	15	*B* 66–80
Totals	49	12	3	5	4	7	80	

* = includes 1 haemoperitoneum, 3 retroperitoneal haematomata as only finding at operation
(C) = Missile penetrating thorax (13 cases)
(P) = Peritonitis present at operation (12 cases)
(G) = Gas gangrene present at operation (1 case)

and necropsy were so varied that few cases were alike They ranged from relatively minor lesions, such as a small bruise of the gut wall, a small haemoperitoneum or a retroperitoneal haematoma without obvious injury to the viscera, up to gross and multiple lacerations of both large and small intestines and of the solid organs These lesions, summarised in Table 21, are divided into two main groups, namely those with and those without intraperitoneal perforation of the intestines

Of the 26 patients without intraperitoneal perforation, the gut was uninjured in 16, bruised in 3 and perforated extraperitoneally in 7 In 13 of them other abdominal viscera were also injured

Of the 54 patients with one or more intraperitoneal perforations, 36 had no other abdominal injury, while 18 had injuries to the kidney, liver, spleen, etc in the combinations shown in the table In 12 of these (marked (P) in the table) peritonitis was revealed at operation Because of the state of the peritoneum and of the short interval between the beginning of observation and operation (3 hr in 10 cases, 5 hr in 2) it is assumed that the peritonitis was already present when the cases were first seen

In 13 of the 80 patients (marked (C) in the table) the missile was found at operation to have entered or left the abdomen by way of the chest

In the great majority of the cases the associated damage to the soft tissues and bones of the trunk and limbs was negligible, being assessed as small (less than 1 hand) in 74, moderate (1 to less than 3 hands) in 5, and as large (3 to less than 5 hands) in 1

Examples of these varied injuries follow, others will be found in the case reports in the later pages

Injuries Not Including Intraperitoneal Perforation of the Gut

(*a*) *Case B* 1 Shell wound Entry in right buttock, no exit Large retroperitoneal haematoma round descending duodenum and pancreas Small wound of left lower chest, *non-penetrating*

(*b*) *Case B* [illegible] Mortar wounds Entry wound 1 in diameter over 10th right rib, no exit Very small superficial wound of left side of neck Large tear in liver, haemoperitoneum of about 300 ml

(*c*) *Case B* 14 Grenade wound Large hole in right buttock, fracture of ilium and severance of sciatic nerve, superficial wound on right thigh, 4 in long Right kidney badly torn small tear in liver, haemoperitoneum of about 400 ml

(*d*) *Case B* 16 Grenade wound Entry in mid right axilla over 9th rib, extrapleural course Large extraperitoneal tear of liver, right kidney torn across, large retroperitoneal haematoma, no haemoperitoneum

(*e*) *Case B* 18 Bullet wound Entry in right loin, exit in left epigastrium Severe bruising of upper jejunum, no perforation, no haemoperitoneum

(*f*) *Case B* 20 Bullet wounds Entry wound through anus, exit in right groin, through and through wound in left buttock, small wound of left foot with compound fracture of os calcis Small bruise of terminal ileum, large retroperitoneal haematoma

(*g*) *Case B* 23 Shell wound Small entry wound in right loin, no exit, small wound of right arm Small extraperitoneal hole in posterior aspect of ascending colon, with surrounding haematoma No haemoperitoneum

Injuries Including Intraperitoneal Perforation of the Gut

(*a*) *Case B* 27 Mortar wounds Entry wound in right hypochondrium ⅛ in diameter, no exit wound Two very small superficial wounds of left shoulder and right thigh One minute perforation of anterior wall of stomach No haemoperitoneum

(*b*) *Case B* 34 Shell wound Entry wound to left of umbilicus, no exit wound, intestines protruding Small cut left upper lip, broken tooth Small hole in jejunum, almost complete severance of ileum, haemoperitoneum of 900 ml

(*c*) *Case B* 49 Revolver bullet wound Entry left side of costo sternal notch, exit in left pelvi-spinal angle Two tears in mesentery, two tears across whole diameter of jejunum with two small perforations and two bruises, tear in left ureter, haemoperitoneum of 1 litre

(*d*) *Case B* 54 Missile unknown Small entry wound in right iliac fossa, no exit wound Superficial wound of neck, 2 × 1 in One small hole in pelvic colon, haemoperitoneum of less than 100 ml

(*e*) *Case B* 60 Shell wound One 1-in hole in mid right buttock, wound track passing up through sacro-iliac joint, psoas, transverse colon and liver and entering thorax Large retroperitoneal haematoma behind ascending colon and right kidney and over solar plexus and duodenum Bruising of whole of posterior aspect of ascending colon Haemoperitoneum of about 500 ml

(*f*) *Case B* 73 Missile unknown Entry wound in right lumbar region, large exit wound between umbilicus and xiphisternum, protrusion of intestines Three large tears of ileum, two large tears and much bruising of caecum, large retroperitoneal haematoma, haemoperitoneum of 1 litre

(*g*) *Case B* 79 Mortar wound Small entry wound left flank, no exit Three small holes in stomach and one in duodenum, five small and three large tears in jejunum, three holes in gall bladder, small tear of liver, two holes in and much bruising of transverse colon, haematoma at lower pole of left kidney, haemoperitoneum of over 1 litre

BLOOD LOSS AND BLOOD VOLUME

Using the dye (T1824) method, the blood volume of 54 patients was measured In only 10 instances was this done when the patients were first seen or soon after In the remainder the measurement was made after operation, but in 20 of them the initial blood volume can be back-calculated with more or less accuracy from the measurements after operation The measured and calculated blood volumes are shown in Tables 24 and 25 (pp 120 and 122)

Rough estimates of total blood loss can be made in 51 cases They are derived from the blood volumes measured before and after operation, supplemented by other evidence from estimates of the amount of blood shed externally and into the abdomen and from changes in the composition of the blood Table 22 shows that more than half the patients are estimated to have lost no more than 30 per cent of their blood and half of these no more than 10 per cent Only 8 had lost over 40 per cent. The table also suggests that, as a rule, blood loss from perforation of the intestine is small and that major bleeding arises from the other injuries The injuries, however, are too complex for closer analysis

Blood loss was not easy to estimate before operation In most cases the examination of wounds, dressings and clothes provided little evidence, as bloody clothing had usually been removed and the wounds redressed The wounds of the trunk and limbs were small, so it is likely that little loss was due to them The amount of blood lost into the abdominal cavity could not be discovered from superficial examination of the abdomen An estimate could, however, be made from the amount found in the abdomen at operation, since this followed within an hour or two of initial observation and seldom provoked free bleeding into the peritoneal cavity The amount of blood found in the cavity was usually small, less than 500 ml in terms of

TABLE 22

Estimates of total blood loss from haemorrhage at first observation

Blood loss (percentage of predicted normal blood volume)	Total patients	Patients with intraperitoneal perforation		Patients without intraperitoneal perforation	
		No other visceral lesion	With other visceral lesion	No other visceral lesion	With other visceral lesion
10 or less	15	11	2	2	—
about 20	10	5	1	3	1
20—30	4	2	1	—	1
30—40	8	1	3	2	2
about 40	6	1	3	—	2
about 45	2	—	1	—	1
about 50	5	1	3	1	—
50—60	1	1	—	—	—
Total	51	22	14	[illegible]	7

whole blood But there were exceptions in *Case B* 71 the bloody fluid removed from the peritoneal cavity was estimated from its haemoglobin content to be equivalent to 2,350 ml whole blood, or about 45 per cent of the patient's predicted normal blood volume

As far as the evidence goes, it seems that loss of blood is occasioned mainly, if not entirely, by haemorrhage, loss of plasma to any material degree is unusual in the early stages (For further discussion, see Part IV, Section D)

Initial State

INTRODUCTION

The first two problems were to determine the gravity of the patient's state and to decide whether or not transfusion was required to prepare him for operation The nature and extent of the internal injuries could only be guessed at, but it was clear in most cases that the danger of a peritoneal infection made early operation a matter of urgency and that the operation would involve at least an exploratory laparotomy and might be long and difficult

We were especially interested in the state of the circulation and the factors affecting it We tried to discover whether it was determined mainly, as in patients with injuries to the limbs, by the level of the blood volume, or whether other factors such as reflexes from the injured viscera or infection of the peritoneal cavity were commonly effective, and, if blood volume was the determining factor, whether or not it in turn was dependent mainly on the amount of blood lost by haemorrhage

Seventy-three patients were seen before operation Table 23 shows that they were seen on the whole later than those with limb injuries (see Table 3, p 10) The shortest time between wounding and inspection was ½ hr, and the longest 76 hr over two thirds were seen after between 4 and 18 hr In many cases the interval was sufficient for infection to become established

and, as the table shows, peritonitis was present in half of those with an intraperitoneal perforation of the gut who were seen more than 8 hr after wounding, while in one other gas gangrene had developed in a buttock wound

TABLE 23

Interval between wounding and observation patients with abdominal injuries

Time (hr)		0–2	2 01 –4	4 01 –8	8 01 –12	12 01 –18	18 01 –24	24 01 –36	76	Total
Patients with intra peritoneal perforation	*No peritonitis*	*1*	*7*	*17*	*6*	*5*	—	*2*	—	*38*
	With peritonitis	—	—	—	*4*	*2*	*1*	*4*	*1*	*12*
	Total	1	7	17	10	7	1	6	1	50
Patients without intraperitoneal perforation		—	—	7	5	4	5	2	—	23
	Total	1	7	24	15	11	6	8	1	73

Only a few patients, injured in the neighbourhood, were admitted direct to the hospitals at which we worked The others had already been examined and treated during their passage from the battlefield through Regimental Aid and Field Ambulance Posts Almost all had received morphine soon after being wounded, the dose being $\frac{1}{4}$ gr in about half and $\frac{1}{6}$ gr in the remainder, one case received $\frac{1}{3}$ gr Most had not been allowed to drink since injury Over a half (42) had been transfused and in most of them transfusion was continuing A few had already received atropine or a similar drug in preparation for operation

CIRCULATORY STATE AND BLOOD LOSS

In discussing the initial circulatory state, the 13 patients with established infection will be put aside for the moment and the remainder divided into two groups, those untransfused (29) and those transfused (31)

Untransfused Patients

The majority of patients who had not been transfused had a blood pressure within normal limits (100–140), in one it was above and in five below these limits A normal blood pressure was generally associated with a normal pulse rate, good face colour and warm extremities, while pallor, coldness and tachycardia accompanied a low blood pressure

Estimates of the initial blood volume and loss of blood for 18 of these patients are shown in Table 24 It will be seen that, as in patients with limb injuries, normal blood pressure is associated with the smaller blood losses and with a blood volume above the critical level of about 70 per cent normal

TABLE 24

Initial blood volume and blood loss related to circulatory state
18 *untransfused patients with abdominal injuries*

Patient	Hours after injury	Blood loss (per cent predicted normal blood volume)	Blood volume (per cent predicted normal)	Blood pressure (mm. of mercury)	Pulse rate (per min.)	Face colour	Extremity temperature
B 48 (I)	4½	10 or less	100 (M)	110/70	72	Good	Warm
B 63 (I)	16½	10 or less	100	110/70	92	Good	Warm
B 70 (I)	7	10 or less	100	120/70	96	—	Cold
B 18	20¼	10 or less	100	130/80	80	Good	Warm
B 37 (I)*	27½	10	90	105/90	120	Good	Warm
B 53 (I)†	[illegible]	10	90	120/70	120	Good	Warm
B 36 (I)	7½	10	90	120/80	100	Good	Warm
B 4	11	20	86 (M)	115/70	86	Good	Warm
B 6	8½	20–30	85 (M)	136/85	80	Good	Warm
B 26	10¼	10–20	80–85	118/70	120	Good	—
B 13	13¼	20	80–85	180/70	100	Good	Cold
B 49 (I)	½	20	80	130/85	72	Pale	Warm
B 44 (I)	4	20–30	80	110/70	100	Pale	Warm
B 10	13½	30+	75 (?)	110/80	100	Good	Cold
B 21	7½	40 (?)	70 (?)	80/60	72	Pale	Cold
B 65	4½	40 (?)	60	75/60	120	Pale	Cold
B 24	7¾	50	60 (M)	65/?	120	Pale	Cold
B 58	3¼	50–60	—	55/?	140	Pale	Cold

I = lesions include an intraperitoneal perforation of the gut
* = papaverine ½ gr and scopolamine — gr given 1 hr previously
† = atropine — gr given ½ hr previously
M = measured blood volume (other values are calculated)
? = less reliable values

Pallor and tachycardia are associated with blood volumes below about 80 per cent normal

It will also be noted that the one patient with hypertension had a blood volume of above 80 per cent This again recalls the limb-injury series but here the hypertension must be ascribed to renal damage rather than to emotional disturbance

Case B 13, aged 25, with a small wound in the right loin, was seen 13¼ hr after injury He had received morphine ¼ gr at 3½ and 11 hr after injury and papaverine ½ gr and scopolamine $\frac{1}{150}$ gr 10 min before being seen He had vomited His pupils were much contracted and he was drowsy, his blood pressure was 180/70 and his pulse rate 100 facial colour was good and his extremities were *cold* There was no direct evidence on which to assess blood loss, but from measurement after operation his initial blood volume is calculated to have been between 80 and 85 per cent normal and his blood loss 20 per cent of his total blood

Operation revealed a laceration of the right kidney and a large haematoma near it The kidney was excised During and after operation, at which he lost about 500 ml of blood, he was transfused with two bottles of blood His blood volume measured at 26 hr after injury (11 hr after operation) was 95 per cent normal

Except for a short period of hypotension towards the end of operation and after it, hypertension persisted for several days At 74 hr after injury his blood pressure was still 160/75, it fell to 130/60 24 hr later and thereafter remained normal By the tenth day after injury he seemed well, his blood pressure then was 120/60 and his pulse rate 80

The blood volume of one of the 4 patients shown in the table as having a low blood pressure cannot be estimated, but his recent injury and the amount of blood loss suggest that blood volume was below the critical level All four were pale and cold and three had rapid pulses The slow pulse of the fourth is possibly a reflex effect from his painful perineal injury, since he had fallen while leaping a fence and a sharp stake had entered the anus and torn the rectum

Patients Previously Transfused

When a transfusion had already been started, it was usually continuing slowly when the patients were seen, in a few it had ceased The blood pressure was at least 100 in 20 cases and lower in the remaining 11 Almost all had a pulse rate over 100 and most had pale faces and cold extremities, irrespective of the level of the blood pressure

In patients with injuries to their limbs it was noted that the blood, plasma and serum used for transfusion in Italy were very liable to provoke transfusion reactions characterized by a phase of vasoconstriction followed by one of vasodilatation, which disturbed the relation existing in untransfused cases between circulatory state and blood volume The same disturbance is evident in those patients with injuries to the abdomen (Table 25) who show pallor, cold extremities and a fast pulse, irrespective of the level of their blood pressure or blood volume

The relationship between the blood pressure and the blood volume is confused There are not enough cases to show clearly what we believe to be true, namely that when transfusion is slow and there are no rigors a normal blood pressure is usually associated with a blood volume of about 70 per cent normal or above, and a low blood pressure usually with a lower blood volume Occasionally, however, as in *Case B* 30, blood pressure is low although blood volume is well above this critical level

It is to be noted that Table 25 refers to only 4 of the 11 patients with hypotension, in all 4 the blood volume had been reduced by considerable haemorrhage In the other 7 the blood volume is unknown, but in most of them haemorrhage is calculated to have been at least 30–40 per cent and transfusion was small, while none had haemoglobin and haematocrit readings above normal There is, therefore, no reason to suspect that, in general, hypotension was due to causes other than haemorrhage In *Case B* 25, however, haemorrhage is calculated to have been no more than 20 per cent and was probably less, while transfusion was equivalent to about 20 per cent of the predicted normal blood volume, the circulatory depression here was probably due to exposure to a temperature below freezing for 12 hr after injury

TABLE 25

Blood volume related to circulatory state 12 transfused patients with abdominal injuries

Patient	Time after injury (hr)	Estimated blood loss (per cent predicted normal blood volume)	Transfusion (per cent blood volume)	Blood volume (per cent predicted normal)	Blood pressure (mm of mercury)	Pulse rate (per min)	Face colour	Extremity temperature	Remarks
B 61 (I)	10	10 or less	5 (1P)	100	130/90	—	Pale	Cold	Forearm veins constricted
B 39 (I)	6	35	10 (2P)	94 (M)	120/70	120	Pale	Cold	
B 17	28½	10–20	4 (½B)	90	140/80	120	—	—	
B 30 (I)	14½	45	24 (3B ½P)	88 (M)	75/45	112	Good	Cold	Forearm veins not constricted
B 32 (I)	2½	45	8 (1B)	72 (M)	85/70	106	Pale	Cold	Forearm veins constricted
B 51 (I)	6½	50	13 (2½P)	70	100/?	104	Pale	Cold	
B 80 (I)	3¾	50	17 (2P ½S)	70 (?)	75/?	130	—	Cold	Dark skin
B 71 (I)	5	50	23 (1½B, 2P)	68 (M)	110/80	132	Pale	Cold	2350 *ml* blood in abdomen
B 62 (I)	4½	50	10 (2P)	60	75/30	140	Pale	Cold	
B 34 (I)	11	20	2 (½B)	70+	130/90	112	Pale	Cold	Peritonitis
B 43 (I)	13½	10 or less	20 (1B 2P, ½S)	120 (M)	135/65	104	Pale	Warm	Peritonitis (lips pale)
B 57 (I)	10	10 or less	7 (1B ½P)	103 (M)	120/80	112	Good	—	Peritonitis

I = *Intraperitoneal perforation of gut*
M = Measured blood volume
B = Bottles of blood
P = „ „ plasma
S = „ „ serum

Infected Patients

Infected patients include 1 with gas gangrene and 12 with peritonitis

In the single instance with early gas gangrene (*Case B* 14), who had previously been transfused with only a small part of a bottle of blood, the blood pressure was 64/45 and the pulse rate 140 His face was pale and his extremities were cold He had almost certainly lost at least two litres of blood by haemorrhage, and it is likely that his initial hypotension was associated with a blood volume reduced below the critical level

The 12 patients with peritonitis (all but 3 having been previously transfused), had at this stage little to distinguish them from the other apparently uninfected cases The pulse rate, however, was on the whole faster, all had pulse rates of over 100 and half of 140 or more There was also less vasoconstriction than is usual with hypotension, half had warm extremities and unconstricted veins, and some had a good facial colour

Initial blood volume is known for 3 of the 6 patients with a normal blood pressure (Table 25), it was normal in 2 and probably above the critical level in the third

In none of the 6 cases of hypotension was the blood volume measured initially, nor can it be calculated Nevertheless there is evidence to suggest what later becomes clear, that blood loss through haemorrhage will not by itself account for all cases of hypotension, which is sometimes associated with a blood volume well above the critical level

In *Case B* 31 (blood pressure 60–65/50) initial haemorrhage is calculated to have been 30 per cent, he had been transfused with one bottle of blood His venous haemoglobin was 118 per cent It is probable therefore that in this case the hypotension was associated with a blood volume reduced below the critical level by haemorrhage and plasma loss

In 2 others (*Case B* 72, blood pressure 70/0, and *Case B* 54, blood pressure 95/45) initial haemorrhage is calculated to have been no more than 10 per cent *Case B* 54 had been transfused with one bottle of plasma and a third of a bottle of blood and venous haemoglobin was 97 per cent. It is likely, therefore, that little if any plasma had been lost, and that the hypotension was associated with a blood volume well above the critical level

OTHER FEATURES OF THE INITIAL STATE

The great majority of the patients were mentally clear and many were anxious, only a few were apathetic, drowsy or disoriented, apparently as a result of morphia Many complained of pain, mainly abdominal and not severe, restlessness was unusual Respirations were commonly thoracic in character and shallow, and increased in rate to between 20 and 30 per minute Many were thirsty and a few avidly so the latter included not only those who had lost much blood but also those long deprived of fluids

Factors Affecting the Circulation

These patients provided insufficient material to observe the effects of the other factors noted in the limb series as disturbing the normal circulatory pattern, particularly of the factors arising within two hours of wounding

Such evidence as can be derived from them and from our previous limited experience of abdominal injuries indicates that the circulation is affected by age, environmental temperature, and emotional and nervous stimuli, in the same way as in limb injuries. We know, for example, that emotional hypertension occurs and that pallor may be present although blood loss is negligible. Whether or not, and in what way, reflexes from the injured viscera may disturb the circulation for the first hour or two after wounding remains undetermined; after this period there is little to suggest such a disturbance (*Case B* 13, p. 120, and *Case B* 60, p. 130).

REMARKS

So far as the evidence goes, therefore, it seems that in abdominal as in limb injuries the initial circulatory state is determined mainly by blood volume. This in its turn is determined mainly by the amount of blood lost by haemorrhage, although when infection has developed it may be lowered by plasma loss; in infected cases the blood pressure may be lowered although the blood volume remains above the critical level of 70 per cent normal.

Course Before Operation

INTRODUCTION

The interval between admission and operation, shown in Table 26, ranged from ½ hr. to 24 hr., the average being about 3 hr.

TABLE 26

Interval between admission to hospital and operation: patients with abdominal injuries

Time (hr.)	0–1	1·01–2	2·01–3	3·01–4	4·01–6	6·01–12	24	Total
Patients with intraperitoneal perforation	7	15	12	5	7	3	—	49
Patients without intraperitoneal perforation	4	5	6	4	2	1	1	23
Total	11	20	18	9	9	4	1	72

The chief difficulties of this period lay in deciding whether or not to continue or begin transfusion, and, if transfusion was to proceed, what should be given and in what quantity. For the greater part of the time, being uncertain how to answer these questions, we did not try to influence the decisions but were content to observe the actions of our colleagues. The general rule followed seemed to be that cases with low blood pressure, and also those with normal blood pressure but pale faces, were transfused on the grounds that they were "shocked" or in "poor general condition". Some medical officers preferred to give plasma rather than blood for "shock"; others gave at least two bottles of blood as a routine to all patients with abdominal

injuries on the ground that those so treated did better at operation Glucose saline was given to a few patients Transfusion begun before admission was almost always continued during the pre-operation period

Of the 25 patients with a normal blood pressure untransfused before admission, only 5 were transfused in the pre-operation period, all these had pale faces initially, and 3 had pulse rates under 100 The remainder, all with a good or fair facial colour and about a third with pulse rates over 100, were sent to operation untransfused

Of 16 previously transfused patients whose blood pressure was normal when seen, transfusion was continued in all but 2 whose faces were not pale

All the 22 cases seen initially with a low blood pressure were transfused before operation

In general, patients with a normal blood pressure were transfused slowly and were sent to operation after one or two bottles of blood or plasma had been given Patients with a low blood pressure were transfused rapidly until the blood pressure was restored to normal levels and then sent to operation as soon as a theatre was available

CIRCULATORY CHANGES

Patients with Normal Blood Pressure

Little of note occurred during the period before operation in patients whose blood pressure had initially been normal Those untransfused for the most part reached operation unchanged in state None showed a fall of blood pressure below 100, while a few showed a rise to hypertensive levels when about to undergo operation For example, in *Case B 6* the blood pressure rose from 125/70 to 150/85 when he was transferred to the operating theatre In a few, also, the pulse rate increased following the administration of atropine or a similar drug in preparation for operation A high proportion of those transfused in the period before operation developed transfusion reactions, in some the vasoconstriction persisted until operation, while in others vasodilatation supervened

Patients with Hypotension

The large majority of patients with initial hypotension (including those infected), responded well to transfusion and went to operation with a normal blood pressure Several are of interest as illustrating certain points that can be paralleled in patients injured in the limbs

(a) *Case B* 71 shows that the blood pressure returns to normal when the blood volume is restored to about the critical level

Case B 71 received a penetrating wound of the abdominal wall, to the left of the umbilicus, and a small wound of the right leg

At the Advanced Dressing Station, about ½ hr later, his general condition was bad, he was conscious, cold and sweating, the pulse was imperceptible at the wrist After transfusion of a bottle of plasma he felt better and warmer Morphine ¼ gr was given, a second bottle of plasma was started and he was sent on by ambulance

In the two following cases circulation was improved, but not restored, by transfusion Continuing or renewed internal haemorrhage seemed responsible

Case B 75 received a penetrating wound in the left hypochondrium An hour later he was given morphine $\frac{1}{3}$ gr At $3\frac{1}{4}$ hr after injury, when he was said to be severely shocked, slow plasma transfusion was started and he was sent to hospital by ambulance There at $5\frac{1}{2}$ hr, the pulse was very poor At $6\frac{3}{4}$ hr, when three quarters of the plasma had entered the vein, blood transfusion was started and the first bottle was given over ten minutes

★Seven hours after injury his face was pale, his skin dry and the extremities cold, and the jugular veins were not visible He was very thirsty Quiet and a little drowsy, he was quite conscious and answered questions clearly though rather slowly There was no pulse at the wrist, and the carotid rate was 120, his blood pressure was 45/?

The second bottle of blood, also given over 10 min, improved his face colour, raised his blood pressure to 95/40 and slowed his pulse to 108 He remained quiet and very thirsty At the end of the third bottle, 10 min later, his blood pressure was 100/50 and his pulse rate 100

The second bottle of plasma was then given over 15 min, during which his blood pressure fell to remain about 85/30, respiratory variation of his blood pressure became evident and his pulse rate rose again to 120 He had by then been transfused with three bottles of blood and almost two of plasma, the equivalent of about 33 per cent of his predicted normal blood volume As he did not seem to improve further, internal bleeding was suspected The fourth bottle of blood was begun and operation started 8 hr after injury

Laparotomy revealed about two litres of blood and clot in the abdomen There was free bleeding from a tear in the base of the mesentery ★

For further course see p 159 He was last seen on the eighth day, when he was suffering from malaria and renal failure

Case B 65 was injured by a bullet which entered the right lower chest and left through the right sacrum He was admitted direct to hospital without treatment

When he came under observation, $4\frac{1}{2}$ hr after injury, he was pale, frightened, restless, groaning and in pain He had not vomited His extremities were cold, his blood pressure was 75/60, his pulse rate 120 and his respiration rate 38

★Morphine $\frac{1}{4}$ gr was given intravenously and one bottle of blood transfused over 20 min, after this his blood pressure was 85/60 and his pulse rate 115 The second bottle of blood, given over 15 min, raised his blood pressure to 95/70 the pulse rate was 110 and respirations 36 Examination showed the right side of the abdomen to be rigid and no peristaltic sounds were heard There was no sign of a haemothorax

During the transfusion of a bottle of serum over the next hour he became more dyspnoeic, the respiration rate rose to 55, the right chest became dull and the apex beat was displaced outwards His blood pressure remained unchanged but his pulse rate rose to 145 He was not cyanosed Internal bleeding was suspected transfusion of another bottle of serum was begun and operation was started at $6\frac{1}{4}$ hr after injury

Laparotomy revealed that the bullet had pierced the diaphragm, torn the liver, passed through the hepatic flexure of the colon and torn the right kidney, which was bleeding freely The abdomen contained over 1,200 ml blood and 400 ml was aspirated from the right chest ★

For further course see p 160, he died 43 hr after operation from a bleeding and infected haemothorax

The next patient is thought to have lost about 40 per cent of his blood, yet transfusion of about 20 per cent of his predicted normal volume of blood failed to restore his blood pressure to normal Infection probably played a part in the circulatory disturbance, for operation revealed much dead and

infected muscle in the buttock wound and the patient died not long after operation from gas gangrene

Case B 14 received a large penetrating wound of the right buttock Morphine ⅔ gr was given at 5½ hr after injury At 7 hr his condition was said to be satisfactory, his pulse rate was 88, he complained of abdominal pain and of nausea At 8 hr, however, he was said to be "exsanguinated and shocked", an attempt at transfusion was unsuccessful and the patient was sent to hospital

On arrival, 10 hr after injury, he was very pale and cold He lay quietly except for occasional restless movements of the arms and head, his eyes were closed His blood pressure was 65/45 and his pulse rate 140 ★The forearm veins were so constricted that difficulty was experienced in inserting a needle, and when it was inserted transfusion would only enter the vein slowly under pressure A hot water bottle laid on the forearm caused the veins to relax and transfusion of the first bottle of blood was completed in 20 min The patient was then conscious and mentally clear, complaining of great thirst, his blood pressure was 75/55 and his pulse rate 140 During the transfusion of the second bottle over half an hour, rigors developed and his blood pressure rose temporarily to 100/75 The third bottle was begun, shivering subsided and blood pressure fell to remain about 90/65, with a pul e rate of 128

Operation was begun at 11½ hr (see p 161)

In *Case B* 72 blood loss was slight, no more than 10 per cent of the original blood His blood volume after transfusion is calculated to have been at least 90 per cent of his predicted normal, yet his blood pressure remained low Presumably in this instance the circulatory depression was due to poisoning of the circulatory control by generalized peritonitis

Case B 72, a German prisoner of war, was seen 15 hr after receiving a penetrating wound in the right side of the abdomen and small wounds of the buttocks The only information about his previous state was that at 12 hr he was 'shocked but in fair condition , and that he was then given morphine ½ gr and transfused with one bottle of plasma

He was apprehensive, thirsty and not sweating His face was pale and his extremities cold, his blood pressure was 70/0, he was pulseless at the wrist and his brachial pulse rate was 140 Blood loss by haemorrhage is calculated to have been 10 per cent He retched several times when given a sip of water He asked for a cigarette and smoked it Two bottles of plasma, given over 5 and 16 min respectively, improved his colour, but his blood pressure remained low and his pulse rate fast The fourth bottle of plasma, given over 1 hr, provoked rigors, and his blood pressure rose temporarily to 105/60 When the rigors passed and he became warmer his blood pressure fell back to 60/? He was then rambling Papaverine ½ gr and scopolamine $\frac{1}{150}$ gr were injected intravenously, blood transfusion was started and he was sent to operation 17 hr after injury with his blood pressure 65/40 and his pulse rate 164 ★When he arrived at the theatre, a few minutes later, his blood pressure was 80–90/60

Transfusion before operation was equivalent to about 20 per cent of his predicted normal blood volume, and his blood volume at the beginning of operation is calculated from a later measurement to have been at least 90 per cent of the predicted normal, probably more

Laparotomy revealed less than 500 ml blood in the abdomen and a foul smelling generalized plastic peritonitis ★

For further course see pp 150 and 165 He died 10 hr after operation

Two cases remain in which there is no obvious explanation for the poor response to transfusion, though it is possible that injury to the solar plexus was

responsible in *Case* B 60 In both of them the blood volume after transfusion was well above the critical level and there was no apparent infection

Case B 60, a German prisoner of war, received a penetrating wound of the right buttock Two hours after injury he was given morphine $\frac{1}{4}$ gr Half an hour later he was said to be very shocked and his pulse almost imperceptible, there was no external bleeding At $3\frac{1}{2}$ hr his pulse was still very weak, plasma transfusion was begun and the patient was sent on to hospital

★When he came under observation, $4\frac{1}{2}$ hr after injury, he was pale and his extremities were cold, there was goose skin on his limbs He was mentally clear and said he had no severe pain He was not bleeding externally His blood pressure was 55/?, his radial pulse imperceptible with an apex rate of 108 The forearm veins were so constricted (the weather was hot) that blood sampling was impossible Even the jugular veins were so narrowed and filled so slowly above an obstructing finger that it was impossible to get a sufficient blood sample

At $4\frac{3}{4}$ hr, when the first bottle of plasma was ended, a bottle of blood was transfused over 1 hr, his blood pressure then was 60/45, his radial pulse still impalpable and his carotid pulse rate 124 The second bottle of blood also transfused over 1 hr, raised his blood pressure to 90/60, his radial pulse became palpable at the rate of 120 the face became a little less pale but the forearm veins were still constricted A blood sample, obtained with difficulty, showed his haemoglobin to be 100 per cent

After a second bottle of plasma, given over 40 min, his blood pressure had fallen back to 80/55 and the pulse rate was 128 Transfusion of the third bottle of plasma was begun slowly At 9 hr, when half the plasma had entered the vein, and after the injection of papaverine $\frac{1}{2}$ gr and scopolamine $\frac{1}{100}$ gr, his blood pressure was still 80/60, his pulse rate was 108 and he was a little warmer Operation was begun a few minutes later

The transfusion before operation (two bottles of blood and two and a half of plasma) was equivalent to about 26 per cent of his predicted normal blood volume His blood volume at operation is calculated to have been about 90 per cent normal after the transfusion, and the total blood loss by haemorrhage is estimated not to have exceeded 45 per cent of his original blood

There was a large retroperitoneal haematoma behind the ascending colon, round the right kidney and over the solar plexus and duodenum The liver and transverse colon were torn and the missile had entered the thorax At operation the abdomen contained about 500 ml blood There was no evidence of peritonitis ★

For further course see p 158 He died shortly after operation

In the above case it will be noted that considerable vasoconstriction was present initially and persisted up to the time of operation In the next case, there was initial vasodilatation rather than constriction

Case B 30 received a penetrating wound in the left mid axillary line over the 10th rib and small wounds of the left arm and leg He said he did not faint or lose much blood He got into a car and drove 200 yards to the Regimental Aid Post, where he was given morphine $\frac{1}{4}$ gr 30 min after injury About $1\frac{1}{4}$ hr after injury the dressing of the chest wound was changed, his general condition was good At $4\frac{3}{4}$ hr he was noted to be paler, his blood pressure was 95/65, his pulse rate 108, he was transfused with one bottle of blood and sent on to hospital There, at $5\frac{1}{2}$ hr his blood pressure was 100/60 and his pulse rate 106 Transfusion was continued, a second and a third bottle of blood and one bottle of plasma being given

★At $14\frac{1}{2}$ hr after injury when the bottle of plasma was almost empty, his blood pressure was 75 45 and his pulse rate 112 His extremities were cool (it was hot weather) but the forearm veins were relaxed The radial pulse was soft and easily palpable His face was sunburnt and pink Blood samples were obtained without difficulty and his blood volume was measured and found to be 88 per cent of the predicted normal,

haemorrhage had not exceeded 50 per cent of the total blood Haemoglobin was 82 per cent

After the first bottle of plasma a further 1½ bottles were given over 20 min, his blood pressure then was 65/40 and his pulse rate 108 The fourth bottle, given over 20 min, provoked a reaction with rigors, coldness and pallor, his blood pressure was raised to 80/60 and his pulse rate to 130 Operation was begun at 16¾ hr after injury

After the measurement of his blood volume, the further transfusion was equivalent to about 14 per cent of his predicted normal and the blood volume at the beginning of operation is calculated to have been between 90 and 100 per cent of his predicted normal

Operation showed that the missile had passed through the pleura, diaphragm, spleen and stomach There was no evidence of peritonitis The abdomen contained about 700 ml of blood and the thorax about 600 ml ★

For further course see pp 158 and 172 He died from pulmonary embolism on the seventeenth day

Course During Operation

INTRODUCTION

The remarks made in discussing wounds of the limbs about the difficulty of giving an adequate account and analysis of the events at operation apply with equal if not greater force to abdominal wounds The operative treatment and anaesthesia were more prolonged, difficult and complicated Respiratory and circulatory disturbances were even more common, in fact, quiet respiration and a steady blood pressure throughout operation were the exception rather than the rule Events followed so rapidly on one another that even two observers could hardly note and record all that happened during the administration of the anaesthetic, the exploration of the abdomen and the repair of the damaged parts, and relate it to the changes in the patient's state Therefore, while it is clear that the anaesthetic agent and its administration and the surgical manipulations may profoundly disturb the patient's circulation, the parts played by each in producing the disturbance could not always be clearly distinguished, or separated from the parts played by other factors such as transfusion, infection and blood loss It is clear, however, that the effects of the various depressor factors are more profound and longer lasting in patients whose blood volume is near the critical level at the beginning of operation than in those whose blood volume is well above it

Major Harbord's knowledge and experience of anaesthetics contributed much to the analysis and understanding of the events now to be described

Seventy-one patients were observed All but 7 came to operation with blood pressures of at least 100 The great majority had already been transfused and transfusion was continued Transfusion was begun during operation in 6 of the 20 hitherto untransfused All had previously received morphine some time after wounding and almost all were given atropine (usually $\frac{1}{100}$ gr) or a similar drug shortly before operation

Time of Operation after Injury

The interval between wounding and the beginning of operation, shown in Table 27, ranged between 1 hr and 81 hr, the average being about 15 hr,

or about 4 hr longer than for patients with limb injuries The delay in operation as compared with the latter is not due to a longer period of observation in hospital but to later admission

TABLE 27

Interval between injury and operation patients with abdominal injuries

Time (hr)	1	4–6	6 01 –8	8 01 –12	12 01 –18	18 01 –24	24 01 –36	Over 36	Total
Patients with intra peritoneal perforation	1	9	11	10 (2P)	8 (3P)	3 (1P)	[illegible] (3P)	1	49
Patients without intra peritoneal perforation	*0*	*1*	*2*	*7*	*5*	*4*	*2*	1	*22*
Total	1	10	13	17	13	7	8	2	71

(P) = with peritonitis

Duration of Operation

The duration of operation, from the beginning of induction of anaesthesia to the end of bandaging, ranged from ¼ hr (in two patients not requiring laparotomy) to 4¾ hr, and is shown in Table 28 The average duration was about 1¾ hr, almost twice as long as that for patients with limb injuries

TABLE 28

Duration of operation patients with abdominal injuries

Time (hr)	0–1	1 01 –1 5	1 51 –2	2 01 –3	3 01 –5	Total
Patients with intraperitoneal perforation	11	14	14	5	3	47
Patients without intraperitoneal perforation	*8*	*6*	*4*	*4*	*0*	*22*
Total	19	20	18	9	3	69

Note Two patients who died during operation are omitted

Anaesthetic Agents

Ether was the anaesthetic agent used for the majority of cases

It was the sole agent used to maintain anaesthesia in 34 cases, induction being effected by ethyl chloride in 24, by 'Pentothal' in 7 by cyclopropane in [illegible] and by a mixture of chloroform and ether in 1 In 3 of these cases bilateral intercostal nerve block was added (with procaine or novocaine) and in 1 also bilateral splanchnic nerve block Ether combined with nitrous oxide and oxygen was used for 20 cases, in 3 it was preceded by 'Pentothal', bilateral intercostal block was added in 4 cases (plus rectus sheath block in 2) Ether combined with cyclopropane and preceded by 'Pentothal' was used in 7 cases For the remaining 10 cases ether, cyclopropane, nitrous oxide, chloroform, 'Pentothal', and local blocks were used alone or in various combinations

Operative Procedures

In all but 2 cases operation involved (in addition to the exploration and excision of limb and other soft tissue wounds) laparotomy, examination of the viscera and closure with or without drainage As is shown in Table 29, the gut was sutured in about two thirds of the cases

In a few cases operation was preceded by catheterization and in a few succeeded by bronchoscopy Gastric suction was begun during operation in a few

It is not surprising, in view of the multiplicity of the visceral lesions in some of the cases and of the difficult circumstances in which the operations were conducted, that on occasion important lesions were missed at operation Unsutured perforations of the gut and other lesions not recognized at operation were found in 9 of the 34 patients examined after death In one of these, and in two others, sutured perforations were found at necropsy to have leaked

CIRCULATORY CHANGES

Changes in the circulation occurred in most patients—increase and decrease of the blood pressure, of the pulse rate and of the calibre of the cutaneous vessels, in the same combinations as in those with injuries to the limbs The factors apparently responsible for these changes, so far as they were analysed, also seem the same as in those with limb injuries, so attention is drawn to certain features only

Changes Associated with Respiratory Disturbances

Respiratory disturbances were frequent at operation The most common was a varying degree of obstruction either in the patient's air passages or in the anaesthetic apparatus, caused most frequently by difficulties in the administration of the anaesthetic, but also by vomiting or by surgical manipulation The respiratory disturbances were not fully investigated

Frequently this obstruction produced hypertension *Case B* 62 is an example, showing the speedy subsidence of the blood pressure when the obstruction is removed

Case B 62 The blood pressure was initially low, but was restored by transfusion, blood volume was raised to about 70 per cent normal (see p 126)

He came to operation at 6½ hr with a transfusion in progress his blood pressure was 145/50 his pulse rate 152 and he had warm extremities and good facial colour One bottle of blood was transfused during operation, which lasted 2¼ hr and revealed much blood in the peritoneum, a right haemothorax, a jagged tear in the liver, one small hole in the caecum and another in the transverse colon

Operation consisted of laparotomy, exploration of the viscera suture of the intestines and closure with drainage of the recto vesical pouch The leg wounds were excised and a plaster was applied

Anaesthesia was induced with 0 25 g 'Pentothal' and maintained with cyclopropane, ether and oxygen with Heidbrink's machine

★During the first hour of operation respiratory obstruction developed, due to the accumulation of secretion in the throat The respirations became bubbly and snoring face colour remained good and the extremities warm His blood pressure rose gradually

TABLE 29

Operative procedures

Chief operative procedure	Patients	Additional operative procedures					
		Resection of intestine	Nephrectomy	Splenectomy	Cholecystectomy	Cystostomy or suture of bladder	Suture of diaphragm or pleura
Laparotomy	11	—	2	2	—	—	1
Laparotomy and suture of intestine	30	3	2	—	1	2	2
Laparotomy and colostomy	7	—	1	—	—	2	1
Laparotomy, suture of intestine and colostomy	16	—	—	—	—	—	—
Wound exploration and excision only	2	—	—	—	—	—	—

Two cases who died during operation are omitted

and his pulse rate slowed, varying between 90 and 120 The rise of blood pressure was interrupted for a short time during manual exploration in the region of the liver, when it fell transiently from 160/60 to 140/60 and then quickly resumed its upward course to reach 180/? by the time the peritoneum was closed The mask was then removed and laryngoscopy showed the throat full of frothy secretion, which was swabbed out Respirations became quiet, an airway was inserted, the mask replaced and the anaesthetic continued Within 3 min of removing the mask his blood pressure had fallen to 110/50 and remained at that level during the second hour of operation, in which the closure of the abdomen was completed and the wounds of the leg were treated ★

For further course see p 153 He made good progress and was last seen on the sixteenth day

The second case illustrates the fall in blood pressure that often occurred on removing the anaesthetic mask at the end of operation We have previously remarked that at this time also a fall in blood pressure is possibly due to the removal of some obstruction, but again the causes have not been analysed

Case B 56 came to operation 12½ hr after receiving a penetrating wound in the right lumbar region He had been transfused with three bottles of plasma, one of blood and one of glucose saline, this last had provoked a reaction, and slight shivering continued His blood pressure was 130/80 and his pulse rate 128, his extremities were cold

One bottle of glucose saline was transfused during operation, which lasted 1¾ hr and revealed two tears in the ascending colon and a considerable retroperitoneal haematoma behind the colon Operation consisted of laparotomy, suture of the colon and caecostomy There was little fresh blood loss

Anaesthesia was induced with nitrous oxide and maintained with nitrous oxide, ether and oxygen, bilateral intercostal and rectus sheath blocks were added (40 ml 1 per cent procaine)

★During the injections for the local blocks some respiratory obstruction developed and this persisted throughout operation with a slight inspiratory stridor and deep respirations The respiratory rate remained about 30 per minute His blood pressure soon rose and remained about 160/80 while his pulse rate varied between 100 and 130 At the end of operation, while the skin of the laparotomy wound was being sutured, the anaesthetic mask was removed His blood pressure fell and remained at 105/40, his pulse rate varying between 110 and 120 ★

The further course was difficult, probably because of salt deficiency and alkalosis He was much better when last seen on the twenty-second day (see p 306)

In the next example the blood pressure fell, not when the mask was removed, but when the Boyle's machine was disconnected from the endotracheal tube It fell further when the endotracheal tube itself was removed

Case B 4 came to operation 13¾ hr after receiving four small wounds in the right upper abdominal quadrant and a small exit wound in the right flank His face colour was good and his extremities were warm, his blood pressure was 115/70 and his pulse rate 85 His blood volume was measured and found to be 86 per cent of the predicted normal and indicated a loss of about 20 per cent of the original blood He was given 1½ bottles of glucose saline before operation and the remaining half bottle during it

Operation lasted ¾ hr and consisted of excision of the wounds, laparotomy, exploration of the abdomen, drainage and closure A small retroperitoneal haematoma was the only finding within the abdomen Little blood was lost at operation and his blood volume is calculated to have remained substantially unchanged

Anaesthesia was induced with nitrous oxide and oxygen and maintained with nitrous oxide, ether and oxygen from Boyle's apparatus through a nasal endotracheal tube

★After the tube had been inserted and the mouth packed with gauze respirations were quiet, but they soon became more rapid and deeper and finally gasping and shallow During closure of the laparotomy wound they ceased for about 1 min. but recommenced, still gasping and shallow Meanwhile the blood pressure and pulse rate gradually rose to reach 165/105 and 130 respectively While the patient was being moved about for bandaging the anaesthetic machine was disconnected from the endotracheal tube and the gauze pack removed from the mouth. The respirations remained very shallow, but in 3 min the blood pressure fell to 140/90 and the pulse rate to 110 and 3 min after this when the blood pressure was 135/50 the nasal tube was removed respirations became temporarily noisy and deep After another 3 min, when the respirations had quietened, his blood pressure was 120/70 and he was sent to the ward, his face colour was good and his extremities were warm ★

The further course was uneventful, he was evacuated to Base on the third day

In this example the fall in blood pressure followed a period of hypertension and did not proceed beyond normal levels But not all falls were preceded by hypertension, and some continued to dangerously low levels The suggested explanation is again that during operation the patient is subjected not only to a pressor stimulus arising from the administration of the anaesthetic but also to a depressor factor arising, for example, from blood loss The pressor factor either just balances the depressor, so that the blood pressure remains about normal levels, or is prepotent, so that it rises The removal of the pressor factor allows the depressor to display itself in a fall in blood pressure The following case illustrates

Case B 24 His initial blood volume was 60 per cent normal, low blood pressure was restored to normal and blood volume raised to 80–90 per cent normal by transfusion (p 126)

The patient came to operation 11 hr after injury, his blood pressure was 100/70 and his pulse rate 112, his extremities were warm, his face was flushed and his skin sweating His blood volume is estimated to have been about 80 per cent of the predicted normal A bottle of plasma was transfused slowly during the first 2 hr of the operation and was followed by half a bottle of glucose saline Operation lasted 3 hr and consisted of exploration and excision of the buttock wound, laparotomy, exposure but not suture of the rectal tear colostomy and closure Blood loss during operation was estimated to be sufficient to reduce his blood volume by about 10 per cent, thus bringing it to about the critical level

Anaesthesia was induced with Pentothal 0 25 g and maintained with ether and oxygen administered by Boyle's machine with carbon dioxide absorption an oral airway was inserted The patient was turned on his face for the treatment of the buttock wound

★After the injection of Pentothal his blood pressure fell to 90/60, during the exploration of the buttock wound it fell further to reach 75/45 and his pulse rate increased to 140 Sweating persisted and the extremities remained warm While the bleeding points were being tied and the wound packed respirations became deep with inspiratory phonation, tracheal tug developed, the whole head jerking with respirations His blood pressure rose quickly to reach 110/45 and his pulse rate increased further to 160 The mask was removed and he was allowed to breathe air for a few minutes His blood pressure fell quickly to 65/50 and his pulse rate declined to 140 He was turned on his back an endotracheal tube passed and the airway reinserted The Boyle's apparatus was connected to the endotracheal tube and the administration

of the anaesthetic continued for the abdominal operation His blood pressure ro e again and remained between 115/65 and 120/70 for the remainder of the operation, his pulse rate remained about 140 Respirations continued to be deep with a tracheal tug, the skin flushed and sweating but the extremities gradually cooling At the end of closure of the laparotomy wound, the Boyle s machine was disconnected from the endotracheal tube and his blood pressure fell promptly to 80/55 To make sure that the rise of blood pressure was due to the administration of the anaesthetic, the Boyle's machine was again connected to the endotracheal tube Respiration at once appeared to become obstructed and a marked tracheal tug developed, the head jerking backwards with inspiration, in five minutes his blood pressure had risen to 112/60 and his pulse rate to 140 The machine was then disconnected and a minute later his blood pressure was 75/50 and his pulse rate 128, respirations had quietened His blood pressure remained about that level for the next ½ hr while bandaging was completed and a bottle of blood was transfused ★

For further course see pp 156, 171 He developed a pararectal abscess (due to a retained swab) and bronchopneumonia, and died on the fourteenth day

Gross respiratory obstruction with deep cyanosis for a period of about three hours led to the death on the table of one patient with a relatively minor injury and apparently little blood loss For the first part of the time the obstruction was associated with hypertension, tachycardia and hyperpnoea, and later with a falling blood pressure, slowing and irregularity of the pulse and gasping and irregular respiration

Case B 3 received one small wound of the right hand and another below the right costal margin in the posterior axillary line

At 2¼ hr after injury his general condition was good, he was given morphine ¼ gr and 2,000 units antitetanic serum At 7 hr his condition was still good, there was neither abdominal rigidity nor distension X-ray examination revealed a small metal fragment near the 3rd lumbar vertebra At 14 hr he was given papaverine and scopolamine

At 17¼ hr he was mentally clear, his pupils were small and his mouth was dry, he had a good face colour and warm extremities, his blood pressure was 130/85 and his pulse rate 120 He was not transfused

Operation, begun 18½ hr after injury, lasted about 3 hr and consisted of laparotomy, exploration and closure The only injury found was a retroperitoneal haematoma behind the right kidney and the hepatic flexure of the colon

★Anaesthesia, induced with nitrous oxide and oxygen and maintained by these agents with the addition of ether through Boyle s apparatus, was light

Respiratory obstruction soon developed and persisted, with hypertension, tachycardia and deep cyanosis Ten minutes after beginning induction his blood pressure was 165/70 and his pulse rate 146, while his respirations were 40, he was sweating profusely, cyanosed and frothing at the mouth He continued in this state while operation was continued with difficulty because of inadequate muscular relaxation and distension of the gut At 1½ hr after beginning induction, when exploration was complete, he was deeply cyanosed, his blood pressure was 150/90, his pulse rate 160 and his respiration rate 48 The mask was removed, the tongue pulled forward and a stomach tube passed, but these measures failed to relieve either respiratory obstruction or gut distension The administration of the anaesthetic was resumed and closure of the abdomen proceeded slowly and with difficulty over the next 1¼ hr During this time gross cyanosis persisted and the respirations became gasping and irregular, his pulse rate slowed and became irregular and his blood pressure fell to 110/75 At the end of the operation respirations ceased and the patient died ★

There was no necropsy

Changes Due to the Pharmacological Properties of the Anaesthetic Agents

In patients with wounds of the abdomen, as in those with wounds of the limbs, ether, cyclopropane and chloroform caused vasodilatation, while "Pentothal" did not seem materially to affect the calibre of the cutaneous vessels The pulse rate was increased by ether, unaltered or a little slowed by cyclopropane, and greatly slowed by chloroform Although the vasodilator properties of ether and cyclopropane might be expected to cause a lowering of the blood pressure, and although blood pressure did in fact generally tend to fall during operation, we have no clear evidence to show that this was due to these anaesthetic agents It is, however, clear that chloroform markedly lowers the blood pressure, this is shown by the following instance, which also illustrates hypertension provoked by respiratory obstruction due to vomiting

Case B 49 was seen ½ hr after being wounded by a revolver bullet which entered by the left costo-sternal notch and left by the pelvi spinal angle The abdominal injuries revealed at operation were two holes across the whole diameter of the jejunum near the duodenum two other small holes and two bruises of the jejunal wall and two bleeding tears of the mesentery A tear of the left ureter, not detected at operation was found at necropsy The total blood loss is calculated to have been no more than 20 per cent The patient was pale his nose and ears warm, his blood pressure 135/55 and his pulse rate 72, the pulse was thin He was given papaverine ½ gr and scopolamine $\frac{1}{150}$ gr intravenously and was sent to operation at 1½ hr after injury, less pale, but with cool fingers and constricted forearm veins His blood pressure was then 130/85 and his pulse rate 72 His blood volume is calculated to have been about 80 per cent normal A transfusion of plasma was running slowly

Operation lasted 1¼ hr and consisted of laparotomy through an infra-umbilical incision exploration of the abdomen, repair of the intestinal lesions and closure The abdomen contained about 1000 ml blood The remainder of the first bottle of plasma and two bottles of blood were transfused during operation At the end of operation his blood volume was calculated to be about 100 per cent normal

★Anaesthesia was induced with "Pentothal" 0 5 g and then an endotracheal tube was inserted, the pharynx packed and anaesthesia continued with chloroform oxygen and nitrous oxide through Boyle s apparatus His blood pressure fell rapidly and his pulse rate slowed in 4 min while the abdomen was being prepared, they reached 50/30 and 64 respectively The face was well coloured The abdomen was then opened and the intestines inspected Meanwhile his blood pressure fell to 40/? and the pulse became barely palpable its rate still about 40 His blood pressure then recovered a little to remain between 55 and 65 until chloroform was withdrawn (15 ml was used) and the laparotomy wound closed There was no cyanosis, the face and fingers remained well coloured, the fingers were cool

For 16 min. after the withdrawal of the chloroform, carbon dioxide and oxygen were given while dressings were being completed By then his blood pressure had risen to 90/60 and his pulse rate to 84

The Boyle s machine was disconnected from the endotracheal tube and the pharyngeal pack and the endotracheal tube were removed, the patient vomited and inhaled vomit ceased breathing and became deeply cyanosed His blood pressure rose to 200/110 and his pulse rate to 140 the pulse being irregular (? extrasystoles) After the insertion of an airway and artificial respiration with oxygen, breathing was restored, cyanosis disappeared and the blood pressure subsided, ¼ hr later, after further vomiting, it was still 165/70, but his pulse rate was 116 ★

The patient died later from bronchopneumonia (p 171)

The use of chloroform for induction is probably responsible for the transient vasovagal-like depression seen in another case

Case B 19 came to operation 24 hr after being wounded His injuries were two small wounds of the right thigh, one of the left arm and three of the right buttock, one leading to the rectum and the others penetrating the pelvis Operation revealed a retroperitoneal haematoma behind the bladder and haemorrhage into the wall of the bladder, which, however, was not ruptured The rectum was intact His colour was good and his extremities were warm, his blood pressure was 105/70 and his pulse rate 92 He had not been transfused

Operation lasted 1¼ hr and consisted of exploration and excision of the wounds of the buttock and limbs, laparotomy through a mid line infra umbilical incision, exploration, colostomy of the descending colon and drainage of the bladder One eighth of a bottle of blood was transfused during operation

★Anaesthesia was induced with a chloroform ether mixture by open mask and then maintained with ether through an endotracheal tube by an Oxford vaporizer

Soon after beginning induction his blood pressure had fallen to 70/? and his pulse rate to 60, respirations were quiet Ether was started and operation proceeded The blood pressure rose gradually, reaching 110/70, and the pulse rate was 90 by the time the peritoneum was closed and the anaesthetic withdrawn His colour remained good and his extremities warm He left the theatre 20 min later with his blood pressure 100/45 and his pulse rate 72 ★

A transient hypotension followed operation (p 153) He made good progress and was followed to the eighth day

A fall of blood pressure followed the production of bilateral intercostal and splanchnic block in two and possibly also in the third of the three patients in whom these local anaesthetic measures were employed Since no fall attributable to the local anaesthesia occurred in eight other patients with bilateral intercostal block (and rectus sheath block in three), the depression of blood pressure is probably to be attributed mainly to the splanchnic block and the concomitant handling of the patient For example

Case B 10 came to operation 14½ hr after injury He had an entry wound ½ in in diameter over the 10th left rib in the mid axillary line leading to a hole through the pleura, diaphragm and spleen, a small piece of metal was found in front of the 1st lumbar vertebra The peritoneal cavity was found to be full of blood and there was also a retroperitoneal haematoma His blood loss is calculated to have been between 30 and 40 per cent of his total blood No transfusion had been given His face colour was good, his extremities were cool His blood pressure was 110/80 and his pulse rate 100 Operation lasted ¾ hr and consisted of laparotomy through a left subcostal incision, exploration of the abdomen, splenectomy and closure Little fresh bleeding occurred One bottle of blood and part of a bottle of plasma were transfused during operation His blood volume is calculated to have been about 75 per cent normal at the beginning of operation and about 70 per cent at the end

★General anaesthesia was induced and maintained with "Pentothal (1 8 g), oxygen was administered through a nasal tube Seven minutes after beginning Pentothal , when 0 5 g had been injected, the lower intercostal nerves on both sides were blocked with 20 ml procaine on each side, the injection occupying 15 min His blood pressure at the start and finish of the injection was 105/80 and his pulse rate 130 The injection of 30 ml procaine on each side for splanchnic block occupied 5 min , at the end of which time his blood pressure was 95/70 and his pulse rate 160 During the next 25 min , while the abdomen was prepared and catheterization carried out, his blood pressure fell to 85/40 and his pulse rate to 130 The abdominal muscles were well relaxed When the peritoneum was opened, his blood pressure fell to 75/40 and remained at that level during the exploration of the abdomen and the mobilization of the spleen Blood transfusion was then speeded up and during the next 20 min , while the spleen was removed and the peritoneum closed, his blood pressure rose to 105/70, his pulse rate to about 140 ★ By this time the effect of local anaesthesia was

passing off and the muscles were tightening Difficulty was experienced in the suturing and while it was in progress his blood pressure fell for a time being 80/60 at the end of operation, the corneal reflex was then positive The blood pressure soon recovered For later course see p 155

Changes Due to Surgical Manipulation

We have seen that, in patients with wounds of the limbs, the surgical manipulation of the injured parts during operation, the movement of the patient during preparation for operation and the bandaging after it may all cause blood pressure either to rise or, more frequently, to fall, and that these effects are usually slight and transient but may be serious and enduring Similar effects may also be provoked in abdominal cases by the handling of the patient before and after operation such procedures as "scrubbing up" the tender abdomen, turning the patient on his side, catheterization and proctoscopy, laryngeal intubation, bronchoscopy and bandaging have all been noted as followed by blood pressure changes For example

Case B 21 fell on a sharp stake which tore the rectum Blood soaked his trousers and ran on the ground Three quarters of an hour later he was given morphine ½ gr

Seen 7½ hr after injury, he was pale and cold, his blood pressure was 80/60 his pulse rate 72 Blood loss and blood volume at that time were calculated to have been about 40 and 70 per cent respectively of the predicted normal

Transfusion of part of a bottle of blood accompanied by rigors, and of one bottle of plasma restored his blood pressure to 110/60 his pulse rate was then 84 He remained pale and cold and was sent to operation 10 hr after injury

★Proctoscopy just before the induction of anaesthesia with Pentothal (0 45 g) caused considerable pain the blood pressure was raised temporarily to 160/80 and the pulse rate to 140 With the patient in the lithotomy position after anaesthetization the buttock wound was opened widely and the contaminated tissues excised, the blood pressure remained about 115/70 the pulse rate 116 During bandaging the blood pressure fell to 85/40 and the pulse rate increased to 160 Four minutes later, when bandaging was completed, the blood pressure had risen to 95/60 and soon rose to 130/70 while the pulse rate declined to 130 ★

The wound became septic but his general condition was good when last seen on the fifth day

Surgical manipulation within the abdomen may also affect the circulation, but because of the difficult circumstances of operation we did not analyse these effects very closely It was difficult, not only to follow the rapidly changing manipulations of the viscera as the surgeon explored the abdomen, but also to estimate the blood pressure sufficiently often to determine the beginning and the course of a change and, hardest of all, to determine which of the manipulations was responsible for the change Manipulation also sometimes disturbed respiration, which might in turn affect circulation

Sometimes manipulation seemed not to affect the circulation at all In some cases the blood pressure remained materially unchanged though the viscera were much and roughly handled The reaction varied even in the individual a manipulation such as traction on the mesentery of the small intestine appeared at one time to provoke a transient fall of blood pressure, but when repeated later to be without effect

The degree of the disturbance may well depend on a number of factors, not only on the particular viscus and the way in which it is handled, but also

on the extent of the visceral injury, the depth of anaesthesia at the time, the patient's blood volume and the presence or absence of infection There are not sufficient comparable cases to allow the parts played by these and other factors to be disentangled We therefore illustrate by example the changes observed and indicate the interpretations suggested by our evidence

There is no doubt that surgical interference in the abdomen frequently provoked a fall of blood pressure So far as the analysis goes, it seems that the particular manipulation most likely to lower the blood pressure was traction on some viscus, but sometimes traction on the abdominal wall seemed effective, while clamping, cutting and suturing the intestine apparently produced no effect For example, a fall of blood pressure was observed to follow quickly on pulling the small intestine from the abdomen for inspection, on traction on the mesentery of the small intestine to expose the pylorus, on pulling on the stomach, on traction on the colon during its mobilization or while bringing it through a stab wound for colostomy and on pulling and retraction in the bladder region The degree and duration of the fall varied considerably, usually it fell 10–20 mm Hg within a minute and then rose more gradually For example, in *Case B* 8, the manipulations of pulling the colon inwards, pulling the duodenal flexure and mopping the paracolic gutter each provoked a transient fall of about 15 mm Hg, the blood pressure falling within a minute and returning to its previous level two or three minutes later In other less usual instances the blood pressure fell when the abdomen was opened or soon after and remained low, perhaps falling further during exploration and repair of the viscera, until closure of the abdomen, during which it rose to about its initial level

Case B 1, first seen 7½ hr after injury, was pale and his extremities were warm, his blood pressure was 105/70, his pulse rate 80 His injuries were a small wound of the left lower chest (the pleura not being perforated) and a second in the right buttock Operation revealed a large retroperitoneal haematoma round the descending duodenum and pancreas a small piece of metal lay medial to the right kidney Blood loss is calculated to have been more than 40 per cent, the initial blood volume is unknown but was probably at least 70 per cent normal One bottle of plasma was transfused before and half a bottle during operation

Operation, begun at 10½ hr after injury, lasted 1½ hr and consisted of exploration and excision of the chest and buttock wounds, laparotomy through a right paramedian incision, drainage through an oblique incision in the right flank and closure of the abdomen Anaesthesia was induced with ethyl chloride (24 ml) and maintained with ether (200 ml) and oxygen by an Oxford vaporiser through an endotracheal tube Except for some straining at intubation, anaesthesia proceeded smoothly Before induction the blood pressure was 120/60 and the pulse rate 90, the patient was warm and sweating No transfusion had been given

★After the buttock and chest had been treated and the patient turned on his back, his blood pressure was 130/90 and his pulse rate 120 His blood pressure remained unchanged as the peritoneum was opened, but when the abdominal wall was retracted and the small intestine pulled out and to the right the blood pressure fell to 90/60 and the pulse rate increased to 132 During the next 2 min the intestine was replaced and the incision extended, the blood pressure rose to 120/70 and the pulse rate fell to 125 During the next 15 min , while the abdomen was explored, blood pressure fell to remain about 105/70, while the pulse rate was 132 Inspection over, his blood pressure rose to remain about 110/60 During the next 20 min , while the foreign

body was removed, the flank incised for draining and the abdomen closed, his blood pressure rose to remain at 125/60 and his pulse rate slowed to 120 ★

He was evacuated to Base on the thirteenth day

Case B 78 received a small wound in the left costal margin leading to the peritoneum, where operation revealed severed and bleeding gastro-epiploic vessels, four perforations in the jejunum and a tear in its mesentery with bleeding vessels, a tear in the left half of the transverse colon and a small through and through wound of the liver (not bleeding) The metal fragment causing the injuries had lodged retroperitoneally lateral to the common iliac vessels The peritoneal cavity contained at least 1,000 ml of blood, a further 250 ml were lost at operation

He had been given morphine ½ gr soon after injury and at 6½ hr after injury was transfused a bottle of blood At 7½ hr his general condition was poor , his blood pressure 90/70, and his pulse rate 120 When seen at [illegible] hr his sunburnt face was of good colour and his extremities warm He was mentally clear and thirsty, his tongue dry and furred The abdomen was rigid and tender Blood pressure was then 100/75, pulse rate 132, *haemoglobin 114 per cent Transfusion of the second* bottle of blood was begun slowly (to be completed over 2 hr) and atropine $\frac{1}{100}$ gr was injected intravenously

Operation, begun at 9¾ hr , lasted 2 hr and consisted of laparotomy, thorough exploration of the viscera, suture of the intestine, mesentery and severed vessels and colostomy in the left hypochondrium The metal fragment was not removed

A nitrous oxide, ether and oxygen mixture was used, bilateral block of the four *lower intercostal nerves was added but proved to be incomplete*

★After anaesthetization and preparation of the abdomen his blood pressure was 125/90 and his pulse rate 120 When the surface wound was excised and the abdomen opened, the radial pulse became impalpable and the blood pressure unmeasurable the carotid pulse rate rose to 136 Though the radial pulse remained barely or not at all palpable throughout operation, the blood pressure soon rose to vary between about 50/? and 60/? over the next half hour, while the viscera were explored and the lacerations sutured *His hands became colder Transfusion of the third bottle of blood* was then begun slowly During closure of the abdomen his blood pressure rose to 80/60, his radial pulse became more easily palpable at about 100 and his hands became warmer When the anaesthetic was withdrawn, while the skin was sutured and the colostomy secured, his blood pressure fell to 70/50 but returned to 80/60 by the end of bandaging, with a pulse rate of 128, ¾ hr after operation his blood pressure was 120/90 and his pulse rate unchanged ★

He made good progress and was last seen on the ninth day

In some cases the apparent reaction to visceral manipulation was a rise rather than a fall of blood pressure But we have not been able to satisfy ourselves that manipulation was in fact the cause of such rises Often they seemed due mainly to the administration of the anaesthetic, with or without *obvious respiratory difficulty* In one instance where the patient seemed to respond to the handling of the small intestine and omentum and to traction on the stomach by a raised blood pressure, the change can be interpreted equally well as a *mounting hypertension due to* the administration of the anaesthetic, on which are superimposed transient depressions provoked by the manipulations of the viscera

Case B 28 underwent operation 18¼ hr after injury It lasted 60 min and consisted of laparotomy through a right paramedian incision, removal of about 1200 ml of blood and clot, thorough exploration of the viscera and suture of two holes in the anterior surface of the stomach and of a few small holes in *the mesentery Half a* bottle of blood was transfused during operation The blood volume [illegible] calculated

to have been a little above 85 per cent at the beginning and about 85 per cent at the end of operation Anaesthesia was induced with ethyl chloride and open ether and maintained with ether through an Oxford vaporizer

There is no note about the presence or absence of respiratory difficulty during operation The respirations, though counted seldom, apparently remained about 40 per minute and there was no gross cyanosis The patient was warm and sweated throughout

★The general course of the blood pressure throughout the operation was a fluctuating rise from 110/80 to 165/70, the first sharp rise apparently coinciding with the handling of the small intestine when the peritoneum was opened The blood pressure reached its height during the closure of the abdomen at this point ether was withdrawn and the mask removed, the blood pressure fell promptly, reaching 125/70 two minutes later The mask was reapplied and in four minutes the blood pressure had risen to 140/70 Then 5 per cent carbon dioxide was given through the mask and the blood pressure fell quickly to 110/80, the mask was removed The blood pressure remained at about the same level while small superficial wounds of the abdominal wall and buttock were excised and bandaging was completed ★

Infection later developed in the abdomen and chest and the patient died on the ninth day Necropsy revealed gross fibrino-purulent peritonitis and bronchopneumonia

BLOOD PRESSURE AND BLOOD VOLUME

Although we cannot clearly distinguish the separate parts played by the various factors affecting the circulation at operation, yet it seems that in these patients, as in those with injuries to the limbs, the various depressor factors are more liable to cause marked hypotension in those patients whose blood volume is near the critical level than in others There are seven patients, all with intraperitoneal perforation of the intestine but without evidence of peritonitis, who reached operation with a blood volume measured or calculated to have been at least 90 per cent of the predicted normal and who lost but little blood during operation in three of these the blood pressure was well maintained throughout operation, while there were only minor and transient depressions in the other four, at least one of whom suffered much manipulation

Case B 39 injured by a grenade, received small wounds of the scalp, left antecubital fossa, both buttocks, and the abdomen Operation revealed two perforations of the small intestine with surrounding bruising about two feet below the duodenum There was no more than 100 ml blood in the peritoneum Said to have been "shocked after injury he was given morphine ¼ gr at ½ hr and again at 2½ hr after injury, when plasma transfusion was started One and a half bottles of plasma were transfused during the journey to hospital, where he arrived about 4½ hr after injury, his blood pressure was then 125/75 and his pulse rate 112 Plasma transfusion was interrupted and a bottle of glucose saline infused in 10 min This provoked rigors, and his blood pressure rose to 140/70 and his pulse rate to 136 Transfusion of the second bottle of plasma was continued slowly and finished during operation Seen by us at 6 hr he was pale, with cold extremities, mentally clear and a little thirsty, his blood pressure was 120/70 and his pulse rate 120 ★His measured blood volume was 94 per cent of the predicted normal and indicated the loss of about 35 per cent of the original blood

Operation begun at 7 hr, lasted 1½ hr and consisted of excision of the wounds of the buttock and arm, laparotomy through a right paramedian incision thorough exploration of the viscera suture of the gut wounds and oversewing the bruising, and closure and excision of the scalp wound The viscera were much handled

Anaesthesia, induced with 'Pentothal' (0 3 g), was maintained with nitrous oxide, oxygen and ether (100 ml) through an endotracheal tube Atropine $\frac{1}{100}$ gr was injected subcutaneously after induction Anaesthesia was rather deep but the administration proceeded smoothly

Little transfusion was given during operation, less than one fifth of the second bottle of plasma and about one fifth of a bottle of blood The total blood loss at operation was estimated as no more than 300 ml The blood volume at the end of operation is calculated to have been about 90 per cent of the predicted normal After induction of anaesthesia with 'Pentothal', the blood pressure was 120/65 and the pulse rate 120 In the next $\frac{1}{4}$ hr, while the buttock and arm wounds were excised, intubation was carried out and the abdomen prepared, the blood pressure rose temporarily to 160/100 while the pulse rate slowed to 110, but it had returned to 120/70 and the pulse rate to 140 when the paramedian incision was made Vasoconstriction had now given way to vasodilatation, the face was pink, the fingers were warm and the forearm veins were more obvious than previously, dilating readily distal to the sphygmomanometer cuff After incision the blood pressure was 115/65 with a pulse rate of 160, but when the peritoneum was opened and the intestine handled it fell to 100/65, there was much handling of both large and small intestine Three minutes later, however, while the perforations were being sutured, it was 120/70 When the intestine was replaced in the abdomen it was 110/70, and there was a short period of apnoea as the peritoneum was handled During closure of the abdominal wall the blood pressure rose to 135/70 and, while the scalp wound was excised, to 145/75, returning to 120/70 when the dressings were applied, the pulse rate remained about 160 and cutaneous vasodilatation persisted The anaesthetic machine was disconnected from the endotracheal tube and the tube removed while dressings were being completed The blood pressure fell to remain at 100/65, the pulse rate being still 160, for the ten minutes that remained until the patient was sent to the ward Then the blood pressure was 125/60 and vasoconstriction was returning ★

The patient became salt deficient, but was much improved by salt infusions (p 306), he was still improving when last seen on the tenth day

Case B 70 was injured by a mortar bomb, a small fragment of which entered through the left loin and lodged at the root of the mesentery of the descending colon There was one perforation in the upper jejunum and a through and through wound of the pelvic colon There was very little blood in the peritoneal cavity Morphine $\frac{1}{4}$ gr was given at $\frac{3}{4}$ hr At $5\frac{1}{4}$ hr his general condition was good, his blood pressure 130/80 and his pulse rate 88, he was given atropine $\frac{1}{100}$ gr

When he came under observation 7 hr after injury, shortly before operation he was experiencing spasms of severe abdominal pain His extremities were cold, his blood pressure was 120/70 and his pulse rate 96 He was shaved in preparation for operation and his blood pressure rose to 150/65, while his pulse rate fell to 92

Operation begun at $7\frac{1}{2}$ hr, lasted $\frac{3}{4}$ hr and consisted of exploration of the wound, laparotomy through an incision in the left iliac fossa examination of the viscera, suture of the small intestine removal of the metal fragment, pelvic colostomy, and closure of the operation wound Anaesthesia was induced with ethyl chloride and maintained with ether and oxygen

★After induction, during which there was some coughing and struggling his blood pressure was 120/80 and his pulse rate 100 Then, while the entry wound was explored and an incision made in the left iliac fossa, there was a period of respiratory arrest with cyanosis His blood pressure fell to 90/60 and his pulse rate to 84 The skin sweated profusely and the extremities were warm The peritoneum was opened and the injury to the descending colon found, his blood pressure then was 85/55 and his pulse rate 100 During colostomy his blood pressure returned to 100/55 while his pulse rate was 108 During a further examination of the small intestine his blood pressure fell transiently to 70/55 Two minutes later it returned to 100/50 while the small intestine was sutured, then rose to remain about 105/55, with a pulse rate of about 116, while the operation was completed Very little blood was lost during operation and no

transfusion was given His blood volume is calculated from a later measurement to have been about 100 per cent normal during operation *

He made good progress and was last seen on the eleventh day

In the third example there was much damage to the intestine and operation was long, yet no gross depression of blood pressure occurred It is to be noted that much and rapid transfusion did not correct the small fall of blood pressure which apparently resulted from handling the gut

Case B 69, a German soldier, was wounded by a tommy gun, taken prisoner, given morphine ¼ gr and carried to our lines His injuries were small wounds of buttock, calf, knee and thigh, three penetrating abdominal wounds in the left flank and one at the umbilicus Operation revealed 12 holes in the small gut and 2 in the pelvic colon The abdomen contained about 500 ml blood

At the Field Ambulance Post at 1¾ hr his blood pressure was 105/75 and his pulse rate 108 On admission to hospital at 4½ hr he was very pale, cold and pulseless at the wrist His blood pressure was said to have been unmeasurable but 10 min later was found to be 110/80 Blood transfusion was started

At 5½ hr, after transfusion of two bottles of blood, he was very pale and pulseless at the wrists, his extremities were cold and the forearm veins so constricted that a blood sample was obtained only with difficulty He was mentally clear and thirsty, he had vomited and was groaning and in pain His blood pressure was 110/80, apex rate 108 Half an hour later, after the third bottle of blood, he was warmer and had a better colour and less pain The radial pulse was just palpable, its rate 114, the forearm veins were still constricted and the blood pressure was 115/85 The fourth bottle of blood was given over the next 1¾ hr At 6¾ hr he was pale and his extremities were still cold, pain had returned and he was a little restless, his blood pressure was 130/90, his pulse rate 120 He was given atropine $\frac{1}{75}$ gr

*Operation, begun at 7¾ hr, lasted 3½ hr and consisted of catheterization, excision of the abdominal wounds, laparotomy and exploration, suture of the small intestine, colostomy, closure and finally excision of the buttock and limb wounds

Anaesthesia induced with nitrous oxide and oxygen, was maintained with ether through the Heidbrink machine On two occasions during the abdominal operation breathing stopped and artificial respiration was required

After induction and while the abdomen was being shaved, his blood pressure was 115/70 and his pulse rate 126, vasoconstriction had given place to vasodilatation, the hands being warm and the face of a good colour During excision of the abdominal wounds his blood pressure was 105/60 and his pulse irregular (extrasystoles) but his blood pressure soon returned to 115/70 When the peritoneum was opened and the small intestine examined his blood pressure fell to 85/60, while his radial pulse became difficult to feel and increased in rate to 150, his face remained of good colour but his hands became cooler At this point the sixth and seventh bottles of blood were given rapidly, each in 5 min but his blood pressure and pulse rate remained unchanged The eighth bottle of blood was started and given in 20 min Then, at about the end of the second hour of operation, the electric light failed and operation was interrupted for 10 min the blood pressure rose to 105/65 and the pulse rate declined to 126, the radial pulse remaining difficult to feel

During the second hour of operation exploration of the viscera was completed, the gut sutured and the colostomy made The ninth bottle of blood was transfused Anaesthesia for the most part of the time was rather light The general level of the blood pressure was about 110 70 and the pulse rate about 110 The observer noted that each time the surgeon put his hands into the abdomen the carotid pulse diminished in volume and the blood pressure fell, in the intervals between manipulations the blood pressure rose again and pulse volume increased The third hour was occupied with the closure of the abdominal wall and the treatment of the limb wounds At the closure of the laparotomy wound the blood pressure was 115/75 and the pulse rate 110, the radial pulse easily palpable and the face of a good colour, although the hands

remained cool The circulatory changes in the final stages were not followed in detail It was noted, however, that the blood pressure fell for a time to 90/75 and the pulse rate increased to 120 during excision of the limb wounds

The blood volume is calculated to have been at least 95 per cent normal at the beginning of operation and raised to over 100 per cent by the end ★

He died 49 hr after operation (p 160)

In contrast there are four patients, all with intraperitoneal perforation of the intestine, whose blood volumes were calculated to have been between 70 and 75 per cent normal at the beginning of operation In one of these (*Case B* 62) there was considerable and persistent respiratory obstruction throughout the abdominal operation and the blood pressure was maintained at hypertensive levels The other three, however, in whom there was no obvious respiratory obstruction, all showed gross depression of the blood pressure early in the operation In one (*Case B* 38 below), the small amount of transfusion during operation was not enough to increase the blood volume materially and the patient ended operation with his blood pressure still dangerously low In the other two, including *Case B* 71 below, more transfusion was given, sufficient to increase the blood volume to 80 or 90 per cent, and in both of them the circulation was restored by the end of operation

Case B 38 received a wound beneath the left costal margin through which omentum protruded Operation revealed three complete transections and three other tears of the small intestine, a long tear in the mesentery and a wound of the paravertebral muscles with a retroperitoneal haematoma The abdomen contained about 500 ml blood There was no evidence of peritonitis

He had been given morphine $\frac{1}{4}$ gr $\frac{1}{2}$ hr after injury, transfusion of one bottle of blood was started at 2 hr

At $5\frac{3}{4}$ hr his face was very pale, his extremities were cold and his forearm veins constricted, his blood pressure was 120/90, his pulse rate 108 ★ Judging by his clinical state and by a later blood volume estimation, he had probably lost 40–50 per cent of his blood and his initial blood volume was probably about 70 per cent normal A slow intravenous infusion of glucose saline was begun, atropine $\frac{1}{75}$ gr was administered and operation began at 6 hr ★

Operation lasted just under $1\frac{1}{2}$ hr and consisted of laparotomy through a left paramedian incision, exploration of the viscera, resections of two portions of the small intestine with two end to end anastomoses, suture of the tears and of the mesentery, closure of the abdomen, excision of the subcostal wound and insertion of a drainage tube through it

Anaesthesia was induced with nitrous oxide and maintained with nitrous oxide, ether and oxygen (Boyle s apparatus) Except for some hyperventilation throughout probably due to accumulation of carbon dioxide, the administration of the anaesthetic proceeded smoothly

★After induction, the patient was catheterized, the abdomen prepared and opened and blood sucked and mopped from the cavity During the 20 min occupied by these procedures the blood pressure remained at about 130/70 the pulse and respiration rates rising to about 150 and 50 respectively In the next 15 min the small intestine was inspected, each coil being withdrawn from the abdomen and replaced, and the rest of the cavity explored, the blood pressure fell, to vary between 70/60 and 75/60, and the radial pulse became barely palpable, its rate remaining about 160 The face became less pale but the hands remained cold and the forearm veins constricted

Inspection over, the blood pressure rose to remain between 80/60 and 90/70 while the resections, anastomoses and suture of the gut proceeded during the following half hour At the same time saline infusion was stopped, after half a bottle had been given, and replaced by blood transfusion Because of constriction, blood would enter

the veins but slowly The application of pressure to increase the flow resulted in the transfusion apparatus coming apart after less than ½ bottle had been given

In the final 15 min of operation the abdominal wall was closed, the subcostal wound excised, a drainage tube inserted and the anaesthetic withdrawn, and dressings were applied The blood pressure fell progressively to reach about 40/? during bandaging Towards the end of the operation a vein at the left ankle was exposed and blood transfusion restarted Five minutes after operation, when half a bottle of blood had been given, the blood pressure was 70/40 and the pulse rate had fallen to 130 The patient was sent to the ward Thereafter circulation was gradually restored by further slow transfusion ★

He developed gross alkalosis and renal failure with oedema and died on the fourth day Necropsy revealed waterlogged tissues, early peritonitis and bronchopneumonia (pp 172 and 305)

Case B 71 was seen at 5 hr, *hypotension was corrected* by transfusion and blood volume raised to between 70 and 75 per cent normal (p 125)

Operation at 8 hr lasted 2 hr and consisted of excision of the subcostal wound, laparotomy through a right paramedian incision, exploration of the viscera, ligature of torn vessels, suture of the gut, colostomy and closure of the abdomen, followed by excision of the leg wound and ligature of the torn *posterior* tibial artery The amount of fresh blood lost at operation is calculated to have been about 10 per cent of the original blood

★Three bottles of blood, the third, fourth and fifth, were given over 35, 30 and 46 min respectively, and another was started towards the end of the operation The blood volume was remeasured ½ hr after operation, when half of this sixth bottle had been given and found to be 95 per cent of the predicted normal ★

Anaesthesia, induced with ethyl chloride, was maintained with ether and oxygen through the Oxford vaporizer (300 ml ether used) The administration of the anaesthetic was smooth and there was no respiratory difficulty

★After anaesthetization and excision of the entry wound the blood pressure was 110/80 and the pulse rate 144 When the abdominal wall was incised and the peritoneum opened, blood gushed out, the blood pressure fell to 95/60 and then, when the small intestine was pulled out, fell again steeply to 65/50 and remained about this level for the next 15 min while the abdomen was explored, the pulse rate remained about 144, the face and lips were pale and the extremities cold During the following ½ hr, while the gut and vessels were sutured and colostomy was carried out, the *blood pressure rose to remain at about* 75/40 and the pulse rate *declined* to 112 During the next ½ hr, while the abdomen was closed and dressings were applied to the wound, the blood pressure rose to remain at about 85/60, the pulse rate still being 112 The blood pressure *rose* to 100/70 while operation was completed and did not fall when the mask was removed It continued to rise while the blood volume was measured and was 125/85 when the patient was returned to the ward about 1 hr after operation At this time his face was a little less pale, his extremities were warm and his pulse rate was 120 ★

For some days he showed evidence of considerable salt shortage, but gradually improved (p 306), and was doing well when last seen on the seventeenth day

BLOOD PRESSURE AND INFECTION

Another factor that renders the circulation unstable and enhances the effect of the depressor factors at operation is the presence of infection Thus in most of the 12 patients with peritonitis the blood pressure fell to low levels

Case B 47 was injured by a mortar bomb, receiving small wounds of the leg and a small penetrating wound of the left flank ★Operation revealed six holes in the small intestine the coils of which were dilated, reddened and sticky, there was no pus or fibrinous exudate The abdomen contained about 400 ml blood and clot ★

When he was seen at 36 hr after injury his face colour was good, the extremities were cool (the weather was warm) and the forearm veins much constricted He was mentally clear and thirsty, and had had nothing to drink since wounding No transfusion had been given His blood pressure was 95/65 and his pulse rate 152 One bottle of plasma was transfused, atropine $\frac{1}{75}$ gr given intravenously and operation started at $36\frac{1}{2}$ hr, when his blood pressure was 100/70 and his pulse rate 164

Operation lasted 1 hr and consisted of laparotomy through a left paramedian incision removal of the blood and clot, exploration and repair of the viscera, closure of the abdomen and, finally, excision of the leg wound Little fresh blood was lost The second bottle of plasma and part of a bottle of blood were transfused during operation

Anaesthesia, induced with ethyl chloride, was maintained with oxygen and ether (150 ml) through the Oxford vaporizer The administration of the anaesthetic was smooth

★During the opening of the peritoneum and removal of blood and clot, the blood pressure remained about 130/70 and the pulse rate 156 During the examination of the small intestine, when the surgeon palpated the diaphragmatic area around the stomach, the blood pressure fell rapidly to 50/? and the radial pulse became impalpable, the carotid pulse rate was 120 The blood pressure remained about that level and the pulse rate increased to about 160 over the next 20 min while exploration and repair were completed During closure of the abdomen the blood pressure rose to remain for a time at 60/? and finally, when the leg wounds were treated, rose to 80/45, the radial pulse becoming palpable ★

He died 21 hr after operation (p 168)

Two patients died on the table, one (*Case B* 42) during induction of anaesthesia and preparation of the abdomen and the other (*Case B* 40) when the small intestine was withdrawn from the abdomen for inspection Both were incompletely observed

Case B 42, a German prisoner of war, was seen about 25 hr after wounding His injuries were a small penetrating abdominal wound in the left iliac fossa and multiple small leg injuries He had been given two doses of morphine of $\frac{1}{4}$ gr each (it is not known when) and one bottle of blood shortly before being seen His facial colour was fair, his nose warmish and his tongue not furred He was thirsty and vomited after sips of water His blood pressure was 70/45, his radial pulse was impalpable but his carotid pulse was of good volume and its rate 140 He was drowsy and a little disoriented An hour later, after one bottle of plasma, his blood pressure was 115/70 and his radial pulse palpable but thin, its rate 144 An hour later still, at 27 hr, after half of the second bottle of plasma, operation was begun

★Anaesthesia was induced with nitrous oxide and oxygen (4 1 mixture) followed by ether As induction was begun so also was preparation of the abdomen and catheterization

Within a minute or two the patient became cyanosed Nitrous oxide was reduced and then withdrawn, but cyanosis persisted, although to a less degree, the administration of ether was begun, the patient breathing well and without obstruction At this time (8 min after beginning induction) the blood pressure was 90/55 Two minutes later the blood pressure was unmeasurable, the respirations gasping, and the pupils dilated Ether was withdrawn, the patient intubated and artificial respiration maintained with oxygen The patient did not recover ★

Necropsy revealed about 200 ml of purulent fluid in the peritoneal cavity and a perforation of the distal ileum the coils of gut being matted together by fibrinous adhesions The spleen was enlarged Some vomit was found in the trachea and bronchi Both lungs showed patches of collapse, more in the left than in the r... Histological examination revealed many fat emboli in the lungs and a ... number in both brain and kidneys

Case B 40, an Indian soldier, was seen 76 hr after wounding with a grenade little was known about his state and his treatment in the interval Small wounds of the right thigh had been excised under 'Pentothal' at 20 hr, a penetrating abdominal wound had been overlooked Vomiting and abdominal distension had developed, with rapid pulse and low fever, no bowel sounds were heard on auscultation He was given morphine ¼ gr and intravenous glucose saline (quantity unknown) at about 59 hr Vomiting and abdominal distension are said to have become less

At 76 hr the abdomen was slightly distended and barely moved with respiration He vomited small amounts frequently His extremities were cold and his forearm veins constricted, his blood pressure was 130/80 and his pulse rate 140

★Operation was begun at 81 hr with the patient in the head down position, blood pressure was 120/70, pulse rate 170 Anaesthesia was induced with 0 25 g 'Pentothal" and maintained with ether, nitrous oxide and oxygen by Heidbrink s machine through an endotracheal tube Procaine, 40 ml 2 per cent, was injected to produce right lower intercostal and rectus sheath block At the end of injection the blood pressure was 110/70 and pulse rate 160 Fifteen minutes later the abdomen was opened through a right paramedian incision and was found to contain some thin fluid and no blood The small intestine was reddened and distended and its coils were matted together by fibrinous exudate The blood pressure was then still 110/40 Ten minutes later, when the small intestine was pulled out of the abdomen and while the adherent coils were being separated the blood pressure fell rapidly to become unrecordable and the radial pulse became impalpable, the carotid pulse rate slowed to 80 per minute The respirations, costal in type, became gasping and infrequent with a pause after expiration the pupils dilated The mask, pack and endotracheal tube were removed there was no vomit or mucus either on the pack or in the tube A bottle of plasma was given rapidly (in 10 min) into the left external jugular vein but by the end of the transfusion the patient had died Very little blood was lost at operation ★

Necropsy was not allowed Bronchoscopy performed soon after death revealed vomit in the pharynx and vomit and secretion in the trachea No act of vomiting had been noted at operation and the patient was in the head down position throughout

Vasovagal collapse and death seemed associated with the manipulation of the small intestine Fatal collapse of this type has previously been described in a patient with injuries to the limbs and insufficient transfusion (*Case H* 113, p 43)

Data about blood loss and blood volume are lacking in these last three examples and it is therefore not known whether or not reduced blood volume contributed to the circulatory collapse at operation, all three were seen late after injury But it is clear from other examples that in the presence of infection the blood pressure is liable to fall at operation even though the blood volume may be well above the critical level or even normal The fall of blood pressure is not prevented by continuing transfusion Thus there are four patients whose blood volume is calculated to have been about normal during operation, in three of whom, described below, the blood pressure fell considerably *Case B* 72, as already noted, displayed hypotension before operation although blood loss was slight and the blood volume was raised by transfusion to 90 per cent normal At operation, although little blood was lost and the blood volume was raised by transfusion to about 100 per cent normal, the blood pressure fell dangerously low In *Case B* 43, although the blood pressure had been maintained before operation and the blood volume as a result of transfusion remained well above normal during operation, still the blood pressure fell considerably

Case B 72 (p 129) was seen 15 hr after wounding, his low blood pressure was not restored by transfusion, although his blood volume was raised to about 90 per cent normal He came to operation 17 hr after injury ★Blood transfusion was continuing slowly, blood pressure was 80–90/60, pulse rate 130, his blood volume is calculated to have been at least 90 per cent normal One bottle of blood was transfused and little blood was lost at operation His blood volume at the end of operation is calculated to have been about 100 per cent normal

Operation lasted 1 hr and consisted of laparotomy, exploration, suture of nine large tears in the ileum and of one in the mesentery, and exteriorization of the sigmoid colon which was pierced with many holes There was a foul smelling plastic peritonitis

Anaesthesia, induced with Pentothal (0 25 g), was maintained with cyclopropane and ether through an endotracheal tube The administration proceeded smoothly and there was no respiratory obstruction

The blood pressure remained about its initial level until after the peritoneum had been opened It then fell gradually to about 60–70/40 and remained at about that level until the abdomen was closed, after which it rose to 75/40 The pulse rate remained about 130 The extremities were cold and the veins constricted ★

Throughout operation there was a respiratory variation of about 10 mm Hg in the blood pressure Bronchoscopy at the end of operation revealed no obstruction to the air passages but caused the blood pressure to fall to 60/40 The patient was then sent to the ward

He died 10 hr after operation (p 165)

Case B 43 came to operation at 14½ hr after injury after receiving two bottles of plasma, half a bottle of serum and one bottle of blood, a slow transfusion of serum was running, his blood pressure was 130/75, his pulse rate 100, the pulse was wide and the veins were unconstricted, but the face was pale ★His blood volume was measured at 13½ hr and found to be 120 per cent predicted normal and is calculated to have remained about this level during operation Only a little serum was transfused at operation and little blood was lost

Operation lasted 2 hr and consisted of laparotomy, exploration and resection of 6 ft of small intestine perforated in many places There were patches of fibrinous exudate on the intestine The abdomen contained about 500 ml blood and clot

Anaesthesia induced with Pentothal (0 25 g), was maintained with ether and cyclopropane through Heidbrink's apparatus, mask and endotracheal tube

The blood pressure soon fell and remained about 100/60, the pulse rate was about 100 The face was pale throughout and the extremities, previously warm, became cold When the abdomen was closed the blood pressure rose to 125/75 Bronchoscopy was then performed and the blood pressure fell steeply to 65/?, the pulse rate rising to 144 ★ After bronchoscopy, and while small limb wounds were being excised, the blood pressure gradually rose to 90/60 and the pulse rate slowed to 112

He improved for a time, but after a transfusion of plasma (possibly bad) he became very ill and soon died, 56 hr after operation Necropsy revealed generalized purulent peritonitis and bronchopneumonia

In the third case the fall of blood pressure was delayed till the end of operation During operation it was maintained by some respiratory obstruction, but at the end, when the Oxford vaporizer was disconnected, it fell steeply and remained low for some time

★*Case B* 57 came to operation at 12½ hr after injury Operation revealed bruising of the ileum and mesentery and an almost complete severance of the pelvic colon The small intestine was reddened and there were fibrin flakes on its surface The stomach and ileum were distended

He had been transfused earlier with one bottle of blood and some plasma, his blood pressure was 125/80 and his pulse rate 112, he was a little restless and complained of pain Throughout operation, during which no transfusion was given, his blood volume is calculated to have been about 100 per cent normal

Operation lasted 3¼ hr and consisted of excision of the wounds, laparotomy, exploration, suture of the bruised ileum, pelvic colostomy, drainage and closure

Anaesthesia was induced with ethyl chloride and maintained with ether (435 ml) through an Oxford vaporizer and an endotracheal tube

After anaesthetization and during excision of a leg wound the blood pressure fell to 105/70 During the next 1½ hr, while the abdominal operation proceeded, it rose gradually to reach 140/70, the face became increasingly cyanosed, the pulse rate remained about 120 and the extremities remained warm During the last hour, while colostomy was completed and the abdominal wall closed, the face colour improved and the blood pressure fell gradually to 120/70 At the end of operation the vaporizer was disconnected from the endotracheal tube, within 2 min the blood pressure fell and remained at 85/60, with a pulse rate of 110, the face being still well coloured and the extremities warm ★

His blood pressure soon returned to normal, after a period of oliguria and depressed urea clearance he did well (pp 164 and 176)

In the fourth patient the course at operation was complicated by vomiting, inhalation of vomit, persisting respiratory obstruction and cyanosis, the blood pressure varied so greatly with respiration that it was not possible to follow its changes (*Case B 54*, p 165)

Course After Operation

INTRODUCTION

Seventy-six patients were followed after operation until they were sufficiently improved to withstand transportation to Base or until they died The duration of observation, including both survivals and deaths, is shown in Table 30

TABLE 30

Duration of observation after operation patients with abdominal injury

	Time (days)						Total
	Less than 1	1–2	2–3	3–5	5–10	10–22	
Patients	9	3	4	5	30	25	76
Deaths	9	3	4	2	10	3	31

For descriptive purposes the period after operation is divided into earlier and later stages In the earlier period, of about 24 hr in duration, the chief illness was, as in limb injuries, circulatory in origin, both in those who had previously lost much blood and in those who had developed infection In the later period many more patients were seriously ill, they remained ill

longer and many more of them died than was the case in those with injuries to the limbs their illness was complex in origin but arose mainly from the development of infection

EARLY POST-OPERATION PERIOD

Most of the cases left the operating theatre with transfusion continuing slowly When the current bottle of blood or plasma was finished, transfusion was replaced by infusion of glucose saline (5 per cent glucose and 0 3 per cent sodium chloride) Further transfusion was given to a number before or after glucose saline was begun Two thirds of the patients were propped up in bed soon after they had recovered from the anaesthetic and continuous gastric suction was begun Morphine $\frac{1}{6}$ gr or $\frac{1}{4}$ gr was given to many, and the smaller dose repeated four-hourly To prevent or overcome infection, treatment was usually also begun with one of the sulphonamide drugs (usually sulphadiazine) or penicillin or both Many patients who received sulphonamides were given 100 ml of an alkaline solution (4 per cent sodium bicarbonate and 4 per cent sodium citrate) by vein each day, to prevent crystalluria

Circulatory Changes

Recovery from the anaesthetic was associated with the same general features as were shown by patients with injured limbs, and we will not deal with them again examples will be found in the subsequent pages We proceed instead to the description of the circulatory changes, again dividing the patients into three groups according to the level of blood pressure before and during operation Cases in which infection was discovered at operation form a fourth group

Patients with Normal Blood Pressure

There were 26 patients whose blood pressure remained at least 100, except for minor transient depressions, before and during operation Most of them had not lost much blood and over a third had not received transfusion Most of those transfused were given only one or two bottles of blood or plasma, a few three bottles The blood volume at the end of operation was measured or can be calculated for 15 of them, it was at least 80 per cent normal in all and between 90 and 100 per cent normal in 9

In all but 2 the circulation was well maintained throughout the early post-operation period The fall of the blood pressure in these 2 cases was associated with cutaneous vasodilatation and with a blood volume between 80 and 90 per cent normal No reason for the hypotension was apparent and both patients recovered

Case B 17 received a penetrating wound of the right chest external to the nipple with a pneumo-haemothorax a small superficial buttock wound and a small penetrating abdominal wound with two bruises of the ileum and a small metal fragment in the great omentum His condition before operation was good

Operation begun at 28½ hr after injury, lasted 1¾ hr and consisted of excision of the wounds, closure of the pleura, laparotomy oversewing of the gut bruises, and closure of the abdomen Little blood was lost A bottle of blood, begun beforehand was transfused slowly during operation and was followed by a third of a bottle of

plasma The anaesthetic was cyclopropane and oxygen given by Heidbrink's machine

During operation there was a persistent and fluctuating hypertension, 140/90 to 185/110, with slight cyanosis, probably due to some respiratory obstruction On the removal of the mask the blood pressure fell to remain about 110/80

★One hour after operation the blood volume was measured and found to be 89 per cent normal Transfusion had stopped and the patient was recovering from the anaesthetic, moving and groaning occasionally His extremities were warm and he was sweating profusely, his blood pressure was 100–110/70 and his pulse rate 168 Becoming more restless, he was given morphine ¼ gr At 2 hr after operation his blood pressure had fallen to 80/60, his pulse rate to 132, he was lying quietly on his left side, still sweating profusely, his extremities were warm and his face a good colour At 3 hr after operation his blood pressure was 75/50, his pulse rate 132, the radial pulse was difficult to feel, sweating had ceased, his colour remained good and the veins were not constricted

When recovery occurred is not known, but the next morning, 12 hr after operation, his blood pressure was 115/90 and his pulse rate 112,★ by this time a bottle of plasma had been transfused and glucose saline infusion and gastric suction had begun His colour was good and his extremities were warm, he was sweating profusely (it was hot weather) Circulation was thereafter maintained

This patient was probably salt deficient for a time, but he was doing well when last seen on the fourteenth day

Case B 19 had a penetrating buttock wound and a haematoma behind the bladder He came to operation (laparotomy and excision of wounds) at 24 hr, untransfused and in good condition Except for a transient fall, his blood pressure was maintained (p 139)

He was watched for 2 hr after operation while he recovered from the anaesthetic Sweating soon ceased, the blood pressure remained at about 120/80 and the pulse rate about 80, and these levels were maintained when he was propped up in bed His colour was good and his extremities were warm

★When his blood pressure fell is not known, but the following morning, 14 hr after operation, it was 85/55 and his pulse rate had risen to 120, his colour was still good and his extremities were warm, he was sweating (the day was hot) In the interval he had been given seven bottles of glucose saline intravenously Five hours later and without further transfusion his blood pressure had returned to 125/85, his pulse rate was 100, his condition was otherwise unchanged His blood volume was measured and found to be 83 per cent normal ★

Thereafter he made good progress until he was last seen on the eighth day

Patients with Normal Blood Pressure succeeding Hypotension

Twenty-two patients had periods of low blood pressure before or during operation or both, but their blood pressure had returned to normal within half an hour of the end of operation Most of them had lost considerable amounts of blood and all except three had been transfused with at least two bottles of blood, plasma or serum The blood volume at the end of operation was measured or can be calculated for nine of them it was 90 per cent or more in four, between 80 and 90 per cent in three and between 70 and 80 per cent in two

Five of these patients had periods of low blood pressure after operation In the first the hypotension was associated with cutaneous vasoconstriction and a blood volume not far above the critical level

In *Case* [illegible] 62 a low initial blood pressure was restored to normal by transfusion and the blood volume raised to about 70 per cent normal At operation (6½ hr) there

was a tear in the liver and a right haemothorax, holes in the caecum and colon were sutured. Respiratory obstruction caused hypertension (pp 126 and 133)

At the end of operation the blood pressure was 110 60 and the pulse rate 100 the face was pale and the extremities were cool. A bottle of blood was being transfused slowly

★Fifteen minutes later, when he was in bed his blood pressure had fallen to 85-95 45, and by the end of the first hour to 80 50, his pulse rate remained about 108 and the skin vessels were constricted. His respirations were deeper than normal, 12 per min. The oral airway which had been inserted at the end of the abdominal operation seemed to be slightly obstructing respiration and was removed. He recovered consciousness a few minutes later

At 1½ hr after operation when his blood pressure was 90 60, his blood volume was measured and found to be 74 per cent normal. His blood pressure continued to rise and reached 110 50 at 2½ hr by which time half a bottle of blood had been given. His face was no longer pale but the forearm veins were still constricted. Circulation was thereafter maintained.★

He made good progress and was last seen on the sixteenth day

In the second patient the fall of blood pressure was associated at first with vasodilatation and later with constriction and was accompanied by haemoconcentration of unknown cause (perhaps fluid loss or infection) The data are incomplete and his blood volume was not measured.

Case B 52 received a small wound over the right lower costal margin and a second small wound in the right flank through which mesentery protruded.

When seen at 6 hr he had been vomiting and was very thirsty, his blood pressure was 135 85 and his pulse rate 100, his face colour was good and his extremities were warm. Blood transfusion had been started shortly before.

An hour later, when he had been given atropine gr 1/100 and taken to the theatre, his general condition was unchanged but his blood pressure had risen to 170 100, while his pulse rate was still 100 Most of the bottle of blood had been given. His venous haemoglobin was 104 per cent, plasma proteins 7 4 g per 100 ml

Operation, begun at 7 hr, revealed a hole through the liver, gall bladder and pylorus, a metal fragment lay in front of the left kidney The intestines were distended and reddened.

Operation lasted 1¾ hr and consisted of laparotomy, exploration suture of the pylorus cholecystectomy and closure of the abdomen with drainage through the entrance wound. The peritoneal cavity contained about 500 ml. bloody fluid and about 250 ml. blood was lost during operation.

Anaesthesia, induced with "Pentothal" (0 2 g), was maintained with ether through an endotracheal tube by an Oxford vaporizer Lower intercostal block was added (13 ml. 2 per cent. procaine) Anaesthesia was kept at a light plane throughout.

★Throughout operation there was much respiratory obstruction from the accumulation of mucus in the endotracheal tube. The pulse rate was irregular and the blood pressure varied greatly but gradually fell. At the end of operation it was 80 50, the radial pulse impalpable and the face pale and cyanosed, and the extremities were cool. Much mucus was removed by suction and the respiratory difficulty was partly relieved. The blood pressure rose, and 15 min. after operation was about 110 80 with a pulse rate of about 148

Morphine ¼ gr was given 1¼ hr after operation and 1¾ hr later the patient was conscious but drowsy and rambling the face colour was good and the extremities were warm, the blood pressure was 105 70 pulse rate 140, respirations 36 Shortly afterwards when transfusion of the third bottle of blood was ended, glucose saline infusion and continuous gastric suction were begun.

Six hours after operation he was rational sleepy and thirsty, his face was well

coloured and his extremities were warm, but his blood pressure had fallen to 85/65 while his pulse rate had risen to 160

The following morning, 16 hr after operation, his blood pressure was still about the same level and the radial pulse almost impalpable and very fast his face was pale and slightly cyanosed and his extremities were cold, he was sweating slightly (it was warm weather) The venous haemoglobin was 127 per cent, plasma protein 5 4 g per 100 ml Since operation he had been given about 1 litre of fluid by mouth and 1 2 litres glucose saline by vein, he had lost about 180 ml by gastric suction and had passed 300 ml urine He was losing a considerable amount of bile through the drainage tube A bottle of plasma was transfused and the glucose saline continued

Ten hours later he was much improved, his blood pressure was 100/70 and his pulse rate 140, his face colour was good and his extremities were warm He had been drinking freely (3 litres) and in addition to the plasma had received 600 ml glucose saline He had lost a further 180 ml by gastric suction and passed a further 250 ml urine ★

He developed widespread bronchopneumonia and died on the fourth day after injury, disturbance of the salt and water balance probably played a major part in the illness and death (pp 172 and 305)

In the other three patients the hypotension was associated with cutaneous vasodilatation and is unexplained, the blood volume measured in one was not much below normal

Case B 10 had a penetrating wound in his left side through pleura, diaphragm and spleen, he was untransfused and in good condition, with a blood volume about 75 per cent normal Operation at 14½ hr was a splenectomy He had transient hypotension (p 139)

★When he was seen in the ward about ¼ hr after operation, a transfusion of plasma was continuing slowly and his blood pressure was 125/70, his pulse rate was 160 and his extremities were warm, he was not sweating

At 3½ hr after operation, when plasma transfusion was ended and glucose saline infusion begun, he was not yet conscious but was restless, flushed and sweating profusely, his blood pressure was 135/? and his pulse rate 160+, his blood volume was measured and found to be 92 per cent normal

By 12 hr after operation his blood pressure had fallen to 80/50 and his pulse rate to 128, he was fully conscious, but drowsy, restless and pale, although his extremities were warm, sweating had ceased, his mouth temperature was 101 3 F (38 5° C) Glucose saline infusion was continuing, he had drunk well and had not vomited

The following morning, 23 hr after operation, his blood pressure had recovered to 100/60 and his pulse rate was 120, his face colour was good and his extremities were warm, his mouth temperature was 98 4° F (36 9° C) Since operation he had been given three and a half bottles of glucose saline by vein Circulation was thereafter maintained ★

Later he had a pleural effusion (possibly due to infection) the lung collapsed and was re-expanded by aspiration He had low pyrexia with a transient rise of blood urea to 116 *mg* per 100 ml He was last seen on the fourteenth day when he still had a low fever but otherwise seemed well

The fall of blood pressure in the two other patients was similar, their blood volume is unknown

Patients with Hypotension

Eighteen patients had at the end of operation a low blood pressure which persisted longer than half an hour In all except one (*Case B* 60, who died 1¾ hr after operation) the blood pressure recovered sooner or later The

actual hour of recovery is not known in most, for they were not watched continuously beyond the first hour or two after operation In two (*Cases B* 75 and 80) the blood pressure recovered to normal levels in about an hour, in *Case B* 24 recovery was delayed until about 13 hr, in *Case B* 64 till between 14 and 22 hr, and in *Case B* 38 till between 23 and 29 hr

Our observations are insufficient to allow us to determine clearly the factors that delayed recovery Nevertheless, analysis of the available data strongly suggests that one of the most important was a blood volume near the critical level due to inadequate transfusion These patients contrast with those in the previous groups in that in five of the seven for whom it was known the blood volume was calculated to be less than 80 per cent normal, and in one case to be near 65 per cent (*Case B* 29) Moreover, judging by the clinical course in the earlier stages and by the evidence of shed blood and of blood sampling, it can fairly be guessed that in four others it was not far above the critical level In most of the patients with rather low blood volume, slow recovery is associated with inadequate transfusion, as an example see *Case B* 24 below, where further blood loss contributed to the delay In two other patients, better transfused, the blood pressure recovered in about an hour (*Cases B* 75 and 80) *Case B* 80 is given below

Case B 24 At 7½ hr his blood volume was 60 per cent normal, he was transfused and his blood pressure restored, operation at 11 hr consisted of suture of a rectal tear and colostomy, there was renewed hypotension (pp 126 and 136)

★The blood volume at the end of operation is calculated to have been about 75 per cent of the predicted normal, the blood pressure was 75/55 and the pulse rate 116 His extremities were cold and his forearm veins constricted The infusion of glucose saline into the saphenous vein at the ankle was running badly and it was replaced by transfusion of a bottle of blood, which also entered only slowly After the application of a hot water bottle the transfused blood entered the vein freely The bottle of blood was given over 25 min and then infusion of glucose saline was resumed, the blood pressure and the pulse rate remained unchanged and the extremities were still cold He was then returned to the ward and warmed with hot water bottles

As the blood pressure did not rise he was given 1 ml pitressin intramuscularly, this had little effect, the blood pressure rising to remain at 80/60 for the next 45 min and the pulse rate slowing to 104 He was then recovering from the anaesthetic and sweating his respirations were about 20 Six hours later the blood pressure was still only 85/60 and the pulse rate 112, he was mentally clear and very thirsty, the abdomen was soft and not distended, he was pale cold and sweating slightly, the respirations were 30 The dressings over the buttock wound had become soaked with bloody serum, so the wound was packed and redressed Slow transfusion of plasma was begun, but over the next 4 hr most of this leaked into the bed and the blood pressure fell to 60/40, the pulse rate rising to 114, respirations remained at 30, he was still pale, cold, thirsty and sweating (it was hot weather) He was then transfused with a bottle of blood which had been added to a bottle of dried plasma * The blood pressure soon rose to 110/68, pulse rate 128, his colour became good, his extremities warm and his veins relaxed Circulation was maintained.★

He later developed a pararectal abscess, due to a retained swab and bronchopneumonia, and died on the fourteenth day (p 171)

* This was done to increase the protein content of the stored blood so that on transfusion more of the fluid might be retained within the vessels This mixture was repeated subsequently in another case but provoked such a violent reaction that it was not used again.

Case B 80 (Gurkha soldier) A bullet traversed the abdomen, it entered at the tip of the 9th left costal cartilage, tore three holes in the jejunum, almost severed the splenic flexure of the colon, pierced the hilum of the left kidney and the diaphragm near its posterior attachment, traversed the pleura and passed out through the posterior chest wall 2 in from the midline

At ½ hr he was pale and sweating, with a pulse rate of 98, he was given morphine ¼ gr and sent on At 1¼ hr his blood pressure was 80/? and his pulse rate 100, a bottle of plasma was transfused and another started for transit At the next stage, 2¼ hr after injury, transfusion of a bottle of serum was begun and the journey continued

When he came under observation, 4¾ hr after injury, he showed little sign of external blood loss, his blood pressure was 75/? and his pulse rate 132 His pulse was thin and his extremities were cold Two bottles of plasma were transfused, over 12 and 18 min respectively, a blood transfusion was started, and atropine $\frac{1}{100}$ gr was given intramuscularly His blood pressure was then 135/65 and his pulse rate 144 He was mentally clear and thirsty, his extremities were less cold and his lips were not pale His blood volume is calculated from a later measurement to have been probably about 80 per cent or a little more

Operation, begun at 5 hr, lasted 1 hr and consisted of laparotomy, exploration, suture of the intestines (single layer sutures), colostomy and closure The kidney lesion was not then recognized Much blood was found in the peritoneum, 1,200 ml was measured The blood volume is calculated to have been reduced to about 75 per cent normal by the end of operation There was no sign of peritonitis

Anaesthesia, induced with "Pentothal" (0 25 g), was maintained with cyclopropane and oxygen (Heidbrink's apparatus, mask and airway)

During induction, the abdomen was scrubbed vigorously, respirations became slow and then ceased Respiration was maintained by manual compression of the bag on the anaesthetic apparatus until closure of the abdomen His blood pressure at first fell to 90/50 and then rose and remained between 110/50 and 130/70, his pulse rate rising to about 130, his fingers were warm

*When the mask was removed at the end of skin suture his blood pressure fell rapidly and became unmeasurable and his radial pulse became impalpable, his lips were pale and cyanosed and his fingers cold The head of the table was lowered and transfusion speeded, the remaining half of the bottle of blood being given in 10 min and another started (given over 1 hr) Over the next ¾ hr his blood pressure rose gradually to 80/40 and his pulse became palpable at the rate of 132 He was returned to bed, the bed foot being raised about 9 in

His blood pressure continued to rise and an hour after operation reached 100/50 with a pulse rate of 128, he was then coming round from the anaesthetic The second bottle of blood was ended and followed by infusion of glucose saline At 2 hr after operation he was awake, his blood pressure was 100/60 and his pulse rate 120, his extremities were warm, his forearm veins relaxed and his respirations 16 His blood volume was measured and found to be 84 per cent normal Infusion of glucose saline was continued and gastric suction begun *

He died 24 hr after operation (p 159)

The level of blood volume, however, is not the only factor influencing recovery after operation There are two patients whose blood volume was at least 90 per cent normal at the end of operation, in one (*Case B* 30) recovery of blood pressure was delayed till 8–15 hr after operation, while the other died soon after operation The interpretation of these cases is doubtful, but they have already been referred to as exceptional in that their initial hypotension responded poorly to transfusion, their blood pressure remaining low before and during operation The delayed recovery in *Case B* 30 may be associated with the large dose of "Pentothal" (2 g) at operation, while it

seems reasonable to attribute the early death of *Case B* 60 to the asphyxia experienced at operation.

In *Case B* 30 *pre-operative transfusion had failed* to restore normal blood pressure, although the blood volume was raised nearly to normal (p 130)

Operation, begun at 16½ hr, lasted 2 hr and consisted of excision and suture of the chest wound, laparotomy, exploration and suture of the stomach perforation The wound of *the diaphragm through which* blood escaped into the abdomen, was not sutured. The *perforated spleen was not removed, nor were the small limb* wounds treated. There was no evidence of peritonitis

Two thirds of a bottle of plasma and one and a half bottles of blood were transfused *at operation*

Anaesthesia was induced and *maintained with* '*Pentothal*' aided by paravertebral block (procaine and adrenaline), oxygen was given through an endotracheal tube

After induction his blood pressure was 85/50 and his pulse rate 120, *but during* operation *his blood pressure fell to vary with manipulation between 50–75/40–60* With closure of the *abdomen it rose and remained at 85/60,* with a pulse rate of 120 His extremities were then warm and his face colour good.

*His blood volume at the end of operation is estimated to have been still between 90 and 100 per cent normal.

The fifth bottle of blood soon ended and glucose saline infusion was slowly begun. His blood pressure rose gradually and 2 hr after operation reached 95/70, his pulse rate remained at 120 and his face was still well coloured, *although* his extremities had become cool, his *respirations* were 32

At 8 hr after operation he was still unconscious, with a blood pressure of 95/75 and a pulse rate of 118, vasoconstriction had given way to full dilatation, his *radial pulse* being soft and wide, his skin generally warm and moist and his forearm veins relaxed (the venous jugular pressure had not increased), respirations were 24 He was reported to have been very restless for a time and had been given morphine ¼ gr *Only one bottle of glucose saline* had been given since operation, and the second was now started.

Sixteen hours after operation he was sleeping propped up in bed, while glucose saline infusion continued slowly and gastric suction had been begun It was *reported that he had* become conscious earlier, had again been restless and *had* been given *another ¼ gr morphine* His blood pressure remained at 95/50, his *pulse rate* was 112 and there was still vasodilatation. His respirations were 24 and his lips were slightly cyanosed, no adventitious signs were heard over the front of the chest.

By the following morning 32 hr after operation, his blood pressure had risen to 125/70 and was thereafter maintained. His *pulse rate* had increased to 136 and his *respirations* to 42 There were signs of a post-operative complication of the lungs His blood volume, measured 6 hr later, was 98 per cent normal *

He died from pulmonary embolism on the seventeenth day (p 172)

In Case B 60 pre-operative transfusion *had failed to restore normal blood pressure,* although blood volume was raised to 90 per cent (see p 130)

He was brought to the theatre 9 hr after injury Operation lasted 1¼ hr and consisted of laparotomy, exploration, pelvic *colostomy and closure* The only lesion recognized was bruising of the colon A quarter of a bottle of plasma was transfused

Anaesthesia was induced with nitrous oxide and maintained with nitrous oxide, ether and oxygen

*Induction caused asphyxia and convulsions, *followed* by vomiting and inhalation of vomit. The patient's skin and the exposed viscera were grossly cyanosed for about ¼ hr, after which time skin and blood colour became good The respiration rate rose to 44 The pulse rate was at first slowed to 88, then became irregular and finally increased to 148 The blood pressure was maintained between 85–95/50–60 but when the mask was removed at the end of operation it fell to 65/50 His extremities were *then* warm.

In the ward, 20 min later, blood pressure had fallen to 40/? while pulse rate remained at 140 Over the next hour dye was injected and blood samples were withdrawn for blood volume measurement (90 per cent normal, red cell volume 68 per cent, plasma volume 110 per cent normal) Blood pressure rose for a time to 75/35 and then fell, the veins became constricted, the radial pulse almost impalpable, the extremities cyanosed, the respirations gasping The patient died 1½ hr after operation, 11¾ hr after injury ★

Necropsy revealed a large retroperitoneal haematoma and tears of the liver and transverse colon, the missile had entered the thorax, there was vomit in the trachea and right main bronchus, and there were many petechial haemorrhages over the surfaces of the lungs The posterior part of the right upper lobe had collapsed and the right lower lobe was congested The small gut was red in patches, and there were many haemorrhages in the mesentery and petechial haemorrhages in the duodenal mucosa These findings suggest an episode of gross respiratory obstruction, probably from the vomit inhaled at operation The histological findings are also compatible with obstruction to the upper respiratory passages A moderate number of fat emboli was found in the lungs but none in the kidneys or brain

In most of the patients of this group the blood pressure, once restored, was maintained for at least the remainder of the early post-operation period In six the circulation again failed, one recovered (*Case B* 75) and five died, two within 24 hr of operation and three within 48 hr Further haemorrhage accounts for the circulatory failure in three of the cases

Case B 75 At 7 hr the low blood pressure had not been restored by transfusion and internal bleeding was suspected (p 128)

Operation, begun at 8 hr, lasted an hour and consisted of laparotomy, exploration and suture of a tear of the jejunum and of a hole in the mesentery The severed mesenteric vessels bled freely and there was difficulty in arresting haemorrhage The torn transverse colon was exteriorized During operation three and a half bottles of blood were transfused (the fourth to the seventh bottle)

Anaesthesia, induced with ethyl chloride, was maintained smoothly with ether and oxygen through an Oxford vaporizer

After induction his blood pressure was 90/40 and his pulse rate 120 The blood pressure fell during exploration to 50/?, the pulse rate remained about 100 With continued transfusion and closure of the abdomen blood pressure rose to 80/45

★The patient was kept in the theatre for an hour after operation while the remainder of the seventh and eighth bottles of blood were transfused, his blood pressure rose to 110/65, his pulse rate to 112 He was then recovering from the anaesthetic, shivering a little and with a fair face colour

At 10 hr after operation he was mentally alert, pale, cold and thirsty, his blood pressure was 70/40 and his pulse rate 136 He had been bleeding into the bed since operation, it was thought he had bled considerably into the peritoneal cavity and that some blood had escaped externally Since operation, two bottles of glucose saline had been given and also a slow transfusion of part of the ninth bottle of blood Transfusion was speeded, the remainder of the ninth and a tenth bottle were given At 16½ hr after operation his blood pressure was 105/45 and his pulse rate 140, his face colour good and extremities warm Circulation was thereafter maintained ★

On the sixth day he developed malaria, when last seen on the eighth day his blood urea was 160 mg per 100 *ml* and urea clearance under 30 per cent normal

Case B 80 (p 157) At 4¼ hr his low blood pressure had been restored to normal by transfusion and his blood volume raised to about 80 per cent normal Operation was at 5 hr, a torn jejunum was repaired and a torn colon exteriorized (holes in the left kidney and diaphragm were undetected) For a time there was hypotension he was transfused until an hour after operation, and an hour later his blood volume was 84 per

cent normal, his blood pressure 100/60 and his pulse rate 120 Renewed circulatory failure and death 24 hr after operation are ascribed to renewed intra abdominal bleeding and delayed transfusion Peritonitis had also developed

★By 11 hr after operation his blood pressure had again fallen, being 95/40 his pulse rate was still 120, but his respirations had risen to 28 his extremities were cool and his veins a little constricted He was restless yet drowsy (two doses of morphine $\frac{1}{6}$ gr had been given) The abdomen was not distended

His blood pressure continued to fall slowly, tachycardia and vasoconstriction increased and he became so restless that he had to be tied down At 20 hr after operation his blood pressure was only 35/? and his pulse rate about 130 Two hours later his blood pressure was unmeasurable, his radial pulse was impalpable and his respirations were laboured, his head was jerking backwards with each inspiration Transfusion of fresh blood was begun and 1½ bottles were given over the next 2½ hr Neither this transfusion nor the intravenous injection of 100 ml 50 per cent glucose caused any improvement His blood pressure remained unmeasurable, his pulse rate declined and his respirations became infrequent and gasping He died 24 hr after operation, 31 hr after injury

Necropsy 10½ hr after death revealed, in addition to the injuries noted above, at least 1,200 ml (measured) bloody fluid and much blood clot in the peritoneal cavity The source of the bleeding after operation was most probably the unrecognized lesion of the hilum of the kidney, where a large branch of the renal artery was almost severed The posterior aspect of the kidney was deeply torn and there was much extravasation of blood into the perirenal tissues The blood clot in the abdomen was disintegrating and probably infected There was blood stained semipurulent fibrinous deposit on the intestinal surface and an early perisplenitis The jejunal sutures had leaked which was the probable source of the peritoneal infection The left pleura contained 350 ml of heavily bloodstained fluid, arising probably from the injury to the diaphragm and chest wall ★ Both lungs were congested and oedematous but not grossly so, most of the lower lobes was collapsed Histological examination added little beyond revealing the presence of a few fat emboli in the lungs but none in the kidneys or brain

Case B 65 A bullet had traversed thorax, diaphragm, liver, colon and right kidney, seen at 4½ hr he had a low blood pressure which had not been restored by transfusion, and signs of right haemothorax had developed Operation, at 6¾ hr, lasted 1¾ hr, there was free bleeding and haemostasis was not secured, nephrectomy and colostomy were carried out

★The blood pressure was restored within 7½ hr of operation but he then showed increasing circulatory embarrassment from the continually bleeding haemothorax This became infected, and he died 43 hr after operation ★

In one case it is probable that developing peritonitis and excessive blood transfusion were responsible for renewed circulatory failure and death at 49 hr after operation

Case B 69 (p 145) had small limb wounds, three abdominal wounds and many perforations of the intestines, his blood pressure was normal at 5½ hr Operation at 7½ hr, lasted 3½ hr and consisted of laparotomy, gut suture and colostomy, it was accompanied by repeated small falls of blood pressure

★He was overtransfused before and during operation being given nine bottles of blood the equivalent of 63 per cent of his normal blood volume His blood volume, measured an hour after operation was 106 per cent of the predicted normal and indicated that total blood loss by haemorrhage had not exceeded 25 per cent of his original blood The red cell volume was 136 per cent (haematocrit 60 per cent) and the plasma volume 79 per cent normal The plasma was heavily jaundiced ★

At 1½ hr after operation his blood pressure reached 100/80, and his pulse rate was 100, he had not recovered from the anaesthetic

★By 20 hr after operation he was mentally clear and anxious, his face was pale with a malar flush and his respirations were 50 per minute There was no sign of venous congestion nor of cardiac enlargement, his blood pressure was 90–100/75 and his pulse rate 120

By 44 hr he was very ill, cold, sweating profusely and restless, his skin was jaundiced and blotchily cyanosed, the abdomen distended, rigid and tender The respirations remained fast, and a well marked pleural rub was heard in the left axilla The peripheral pulses were impalpable, the heart rate was 160, the blood pressure ? 90/? The heart seemed enlarged, the jugular veins were not visible and did not stand out above an obstructing finger It was thought that he had developed peritonitis and that probably his circulation was being embarrassed by gross haemoconcentration, the haematocrit having risen to 69 per cent ★

An attempt was made to dilute the blood by plasma transfusion and by withdrawing blood Over the next 5 hr five bottles of plasma were given but, owing to gross venous constriction, only about 300 ml blood was withdrawn His condition did not improve, profuse sweating continued and his blood pressure gradually fell and became unmeasurable At 48½ hr the haematocrit was 52 per cent He died 49 hr after operation

★Necropsy, 3 hr after death, revealed early generalized peritonitis ★ The repairs to the intestine were sound and it contained no excess fluid The heart seemed normal There was no pleurisy or gross oedema of the lungs, and only patchy collapse of both lower lobes Apart from congestion of the meninges the brain seemed normal Histological examination showed no abnormality of the kidneys, glomeruli or tubules, many fat emboli were seen in the lungs and a few in the kidneys and brain

Case B 79 Many intra-abdominal lesions were unnoticed at operation Death at 48 hr after operation is attributed mainly to continued gross leakage from a duodenal and gall bladder fistula, there was also early peritonitis (p 305)

Case B 35 was not watched beyond the 3½ hr required for the restoration of his blood pressure, and the cause of the final collapse and death 9 hr after operation is uncertain Necropsy *indicated that it was due to asphyxia from the inhalation of* vomit

Patients with Infections

The 11 patients with infections included 1 with gas gangrene and 10 with peritonitis

In the patient with gas gangrene, the blood pressure was low at the end of operation Circulation did not recover and the patient died 15 hr after operation Although the measurement of the blood volume showed that he had suffered considerable haemorrhage and although he had been transfused with four bottles of blood and one of plasma, the normal process of dilution had not taken place Further transfusion failed to dilute the blood The low blood volume probably contributed to the early death

Case B 14 had a penetrating, infected buttock wound, and his low blood pressure was not restored by transfusion (p 129)

Operation, begun at 11½ hr, lasted 1¼ hr and consisted of laparotomy, excision of the right kidney, removal of a metal fragment from the liver and closure with drainage The large infected buttock wound was considered surgically untreatable and was liberally sprinkled with penicillin powder A bottle of blood (the fourth) was transfused

Anaesthesia, induced with ethyl chloride, was maintained with ether and oxygen

★At the end of operation the blood pressure was 60/?, the peripheral pulses were absent, and the heart rate was 140, the face was pale and the extremities were cold,

the respiration rate was 54 A bottle of plasma was transfused slowly (over 2½ hr) and followed by glucose saline

One hour after operation, the blood pressure had risen to 75/65 the radial pulse was palpable and its rate 180, the face colour had improved and the extremities were warmer, respiration was still 52

By 2½ hr, when he had recovered from the anaesthetic the blood pressure had risen to 90/65, and the pulse rate was 140 The patient was thirsty and pale, his extremities were cool and the forearm veins were so constricted that blood sampling was difficult Hot water bottles applied to the arms relaxed the veins and at 2½ hr the blood volume was measured and found to be 75 per cent normal, indicating the loss of 50 per cent of the original blood The high haemoglobin (101 per cent) showed that dilution had not taken place

The second bottle of plasma was transfused and followed by glucose saline

By 11 hr he was sweating freely and was very restless and mentally deranged, he had vomited several times, the blood pressure was 80/?, the radial pulse impalpable, the carotid easily palpable and its rate 160 Blood sampling showed haemoglobin unchanged

No further transfusion was given and he died 4 hr later, 15 hr after operation

At necropsy, 12 hr after death, the whole body was distended with gas and the tissues stained by haemoglobin No histological examination was made ★

Of the ten patients with peritonitis only two had a normal blood pressure at the end of operation, in four others it rose to normal levels within 4 hr , but in three of them it soon fell again and failed to recover They and the four remaining cases whose blood pressure did not rise after operation all died between 6 and 30 hr after operation Thus only three of the cases with peritonitis passed into the late post-operation period with circulation apparently well restored Only one of them (*Case B* 57, p 150) survived, *Case B* 43 died 56 hr after injury (p 150) and *Case B* 50 on the tenth day, from pneumonia

For the interpretation of the course of these patients our data are incomplete Although data on blood volume are available for eight of them, in none do we know the infecting organism, nor have we any satisfactory gauge of the severity of the infection a rough indication of the latter is given by the interval between wounding and operation and by the appearance of the viscera at operation For example in *Cases B* 57, 31 and 34 the relatively short period of 9–12 hr between wounding and operation and the reddening and loss of lustre of the peritoneum with little or no fibrinous exudate may be taken to indicate an earlier stage of infection than that in *Cases B* 72 and 54, who came to operation at 17 and 23 hr respectively and in whom the coils of gut were matted together with fibrinous exudate Again, the restriction of reddening and exudate to the neighbourhood of the injured part of the gut, as in *Case B* 43 and *Case B* 50, may be taken to indicate an infection more localized than that of the other cases in which these changes were more widespread It is to be remembered, however, that different organisms may provoke differing local reactions and that the local reactions themselves are not a good guide to the severity of the infection for the body generally

Nevertheless analysis of the available data on this basis suggests that, in the early stages of infection, considerable blood loss and reduced blood volume adversely affect the patient's course From this point of view we may compare *Cases B* 31 and 45 with *Case B* 57 They came to operation at 9½, 13½ and 12½ hr after injury respectively *Cases B* 31 and 45 had lost much

blood, so that their blood volume at the end of operation was not much above 70 per cent normal, and they both died soon after, *Case B* 57 lost little blood and had a normal blood volume at the end of operation, and he recovered

Case B 31 received a penetrating wound of the root of the nose, a penetrating wound of the right lower chest with a small haemothorax, perforation of the diaphragm and liver, three perforations of the stomach and one of the spleen

★Seen at [illegible] hr after injury, following the transfusion of one bottle of blood, he was mentally clear and very thirsty, and his tongue was dry and brown, the face colour was moderately good, though the lips were pale, the blood pressure was 60–65/50, the pulse rate 120, the respiration rate 40 and the haemoglobin 118 per cent

Transfusion of two bottles of blood in an hour raised the blood pressure to 100/75 and the pulse rate to 150

Operation, begun at 9½ hr, lasted 1½ hr and consisted of laparotomy, exploration, suture of the stomach and packing and suture of the liver wound The abdomen contained at least 2 litres of blood mixed with food The peritoneum was reddened and there were some flakes of fibrin One bottle of plasma and two of blood were transfused

Anaesthesia, induced with ethyl chloride, was maintained with ether and oxygen through an Oxford vaporizer

On opening the abdomen, the blood pressure became unmeasurable and the radial and temporal pulses impalpable, and they remained so until the end of operation The carotid pulse remained easily palpable at 140 With the fall of the blood pressure respiration ceased, but restarted after a short period of artificial respiration Face colour remained good and the extremities cool The blood volume at the end of operation is calculated to have been a little over 70 per cent normal

After operation no further transfusion was given and only half a bottle of glucose saline infused

At 4½ hr after operation he had not fully recovered from the anaesthetic, his face colour was good, his blood pressure still unmeasurable and his radial pulse impalpable, his carotid pulse was easily palpable at 130 and his respiration rate was 55

At 5 hr, while he was still in the same state, his blood volume was measured and found to be 74 per cent normal, and the haemoglobin had risen to 124 per cent The total blood loss cannot have been more than 45 per cent of his blood It is to be noted that, though at this time the radial and brachial pulses were impalpable and the blood pressure was unmeasurable, the forearm veins filled slowly distal to a cuff at 50 mm Hg The blood pressure must therefore have exceeded this pressure

The patient died 6½ hr after operation, 17 hr after injury ★

Necropsy, 3¾ hr after death, revealed in addition to the injuries noted above that the nasal wound had penetrated the orbit but not the skull Apart from a small subarachnoid haemorrhage in front of and beneath both frontal lobes, the brain was normal There was generalized early peritonitis with much infection, a fibrinopurulent exudate and many petechiae The left pleura contained a small metal fragment and 360 ml. blood and the left lower lobe was collapsed The upper lobe and the right lung were a little congested Histological examination added nothing to the findings beyond a few fat emboli in the lungs, there were none in the kidneys or brain

Case B 45 received small wounds of the left arm and the left iliac fossa Operation revealed a plastic peritonitis without pus, about 900 ml blood in the abdomen and 12 holes in the small intestine

At 2½ hr he was given morphine ¼ gr and plasma transfusion was begun

★Seen at 11 hr after injury, following the transfusion of two bottles of plasma and one and a half of blood, he was pale, his extremities were cold and his blood pressure was 110/90, his pulse rate 140 and his haemoglobin 78 per cent The abdomen was rigid

Before operation the second bottle of blood was finished and the third begun, and at 13 hr he was less pale and his extremities were warm, his blood pressure was 120/90 and his pulse rate 160

Operation, begun at 13½ hr, lasted 1¼ hr under nitrous oxide, oxygen and ether with intercostal and rectus sheath block About 300 ml blood was lost, the third bottle of blood was completed and the fourth and part of the fifth were transfused

After anaesthetization, the face was flushed and the extremities warm When the abdomen was opened, the blood pressure fell steeply from 120/75 to 70/40, while the pulse rate remained about 160 On speeding transfusion and during the resection of 8 in of small intestine and suture of five perforations, the blood pressure rose to 90/60, the face remained flushed When the abdomen was closed, the blood pressure rose to 110/70, but it fell [illegible] 85/65 when the anaesthetic mask was removed, he was then flushed and sweating freely, still with a pulse rate of 160

Soon after operation gastric suction was begun and transfusion continued slowly, the fifth bottle of blood was completed and one of plasma was given in the [illegible] hr for which the patient survived

About an hour after operation, the blood pressure had fallen to 65/?, and the pulse rate was 176, he was sweating and restless, his face [illegible] good colour, the radial pulse barely palpable Methedrine (m 27) was injected intramuscularly and the blood pressure rose a little He regained consciousness 1½ hr after operation

At 4 hr his blood pressure was 85/65, his heart rate about 190, his radial pulse impalpable and his carotid nearly so His face colour was still fairly good and his extremities were cool, he was conscious and rational and felt very tired Jugular venous pressure was not raised His blood volume was measured and found to be 78 per cent normal, indicating a maximum blood loss by haemorrhage of 50 per cent of the original blood In spite of the transfusion of five bottles of blood and two and a half of plasma in the 7 hr since he was first seen, the usual blood dilution had not occurred, his haemoglobin had risen to 105 per cent

He died 9 hr after operation 24 hr after injury ★

Necropsy, 14 hr after death, revealed considerable post mortem degeneration, about 300 ml thin blood stained fluid in the abdomen and a generalized plastic peritonitis The lower lobes of both lungs and the lower portions of the upper lobes were deeply congested and oedematous The subpial vessels were markedly injected, particularly over the frontal and parietal lobes of the brain A few fat emboli were found in the lungs, none in the kidneys or brain

Case B 57 had a gross tear of the pelvic colon and early peritonitis His blood pressure was normal, his pulse fast, and his blood volume about 100 per cent normal Operation at 12½ hr consisted of colostomy, there was increasing hypertension and cyanosis (see p 150)

★At the end of operation his blood pressure fell to 85/60 and his pulse rate was 110, his face colour was good and his extremities were warm, the blood volume was calculated to be about 100 per cent normal He was not receiving transfusion

Half an hour later his condition was unchanged By 10¼ hr after operation he had recovered from the anaesthetic, and glucose saline infusion and gastric suction had been begun His abdomen was distended and he had some cough His blood pressure was 120/80, his pulse rate 104, his respiration rate 24, his extremities were warm and his face was well coloured Circulation was thereafter maintained ★

He seemed well when transferred to Base on the twenty first day (p 176)

The two other patients who, like *Case B* 57, survived the early post-operation period with their blood pressure at normal levels (*Cases B* 43 and 50) had lost little blood and their blood volume was adequate Both came to operation later than Case *B* 57 but in both the inflammatory reaction of the peritoneum appeared confined to the neighbourhood of the injuries

But there are two other cases which suggest that when infection is further advanced gross circulatory failure develops and does not respond to transfusion, and that death follows even if the blood volume is normal The hypotension is associated with vasodilatation rather than vasoconstriction In both cases vasopressor drugs failed to raise the blood pressure *Case B* 72 was over-transfused at the end in an effort to raise the blood pressure, but it still remained low The transfusion did not cause pulmonary oedema

Case B 72 When he was seen at 15 hr his low blood pressure had not been restored by transfusion, although his blood volume had been raised to about 90 per cent normal, operation at 17 hr revealed a foul smelling peritonitis and many tears in small and large intestines Hypotension persisted (pp 129 and 150)

★At the end of operation the blood pressure was 60/40, the pulse rate 130 and the blood volume about 100 per cent normal Plasma transfusion continued slowly

At 15 min after operation, when transfusion ended, the blood pressure had risen to 100/70, the pulse rate was 136 and respiration rate 24, the face was pale and the forearm veins were constricted Fifteen minutes later the blood pressure began to fall and fell slowly until death

At 2½ hr, when he had recovered from the anaesthetic, his blood pressure was 90/50, his pulse rate 140 and his respiration rate 32, his forearm veins were no longer constricted His blood volume was measured and found to be 103 per cent normal, indicating a total haemorrhage of 10 per cent, haemoglobin was 92 per cent Glucose saline infusion, gastric suction and continuous intramuscular injection of penicillin were begun

He became very restless and was given 2 ml paraldehyde by vein, this was ineffective and morphine ¼ gr was given

At 4¼ hr he was quieter, his blood pressure was 75/45 and his pulse rate 140, his extremities were warm and his veins relaxed Injection of 1 mg 'Neosynephrine" intramuscularly failed to raise his blood pressure

At 6½ hr he was restless again, his blood pressure was 55/35, his pulse rate 140 and his respiration rate 40, his face was a little pale and his fingers were cool, but his veins were not constricted A blood sample showed that his haemoglobin had risen slightly, to 97 per cent

At this point 1,000 ml double strength serum (12 g protein per 100 ml) was transfused over 1 hr, but when it was finished his blood pressure had fallen to 50/25, the radial pulse was more easily palpable and the fingers were warmer He was quieter Haemoglobin had fallen to 75 per cent Transfusion of 500 ml normal strength serum was begun, but the patient died at 10 hr after operation (28 hr after injury)

Necropsy, 1½ hr after death, revealed in addition to the injuries noted earlier a generalized fibrinopurulent peritonitis, the small intestine was slightly distended and a sutured perforation of the jejunum was leaking ★ The contents of both large and small intestines were pultaceous The tissues generally were not oedematous The peritoneal cavity contained about 200 ml thin blood-stained fluid, there was a little oedema around the kidneys and behind the caecum ★Both lungs were dry and crepitant The heart was normal ★ Histological examination showed nothing further beyond the presence of a moderate number of fat emboli in the lungs and a few in the kidneys, there were none in the brain

Case B 54, a Gurkha soldier, received a small superficial wound of the neck and a small penetrating wound of the right iliac fossa There was a single perforation of the pelvic colon

★When he was seen at 22½ hr after injury, following the transfusion of a bottle of plasma and a third of a bottle of blood, his blood pressure was 95–100/45, his pulse rate 168 and his respiration rate 28, his extremities were warm and his forearm veins were not constricted His lips were pale Transfusion of two and a half bottles of

plasma over ½ hr raised his blood pressure to 125/50, the pulse rate was 156, the respiration rate still 28, his extremities were still warm and his lips were now pink, his blood volume is calculated to have been about 100 per cent normal ★

Operation, begun at 23 hr, lasted 1¼ hr and consisted of laparotomy, exteriorization of the perforated colon, and closure The peritoneal cavity contained a little thin brown fluid and there was a widespread fibrino-purulent peritonitis Half a bottle of plasma was transfused

Anaesthesia, induced with 'Pentothal' (0 2 g), was maintained with ether and cyclopropane by endotracheal tube and mask and Heidbrink's apparatus

★Early in the operation the patient vomited and inhaled vomit with consequent respiratory obstruction and cyanosis Although attempts were made to relieve the obstruction it persisted throughout operation The blood pressure varied greatly with respiration At the end of operation a bronchoscope was passed and about 20 ml yellowish green frothy mucoid fluid (similar to the vomit in the pharynx) was aspirated from the trachea Respiratory obstruction was relieved and the patient left the table with a blood pressure of 110/60 and a pulse rate of 160, with pink lips and warm extremities Glucose saline infusion was begun

The blood pressure was not maintained for long, at 2 hr after operation it was 90/60 and at 4 hr 85/40 Between these two observations the blood volume was measured and found to be 103 per cent normal, indicating that total haemorrhage had been at most 10 per cent, his haemoglobin was 87 per cent. Methedrine 30 mg, injected subcutaneously, failed to raise his blood pressure To control restlessness, 'Pentothal' 0 22 g was given by vein

At 6 hr, when the blood pressure was 65/40, 100 ml 50 per cent glucose was injected intravenously, this raised the blood pressure to 100/40 for a time and the respirations became bubbly The pulse rate remained about 160 and the extremities warm At 7¼ hr the blood pressure was 70/40 and he was again very restless More 'Pentothal' was given At 8 hr transfusion of double strength serum was begun, but the blood pressure continued to fall and the patient died 8½ hr after operation (33 hr after injury)

Necropsy, 13 hr after death, revealed a generalized fibrino-purulent peritonitis The mucosa of the duodenum and upper small gut was haemorrhagic. The larynx was slightly oedematous and the trachea and main bronchi contained brownish frothy mucus like vomit Both lungs, especially their posterior portions, were congested and oedematous Histological examination revealed early bronchopneumonia and a few fat emboli in the lungs and kidneys ★

It is possible that in addition to the infection, which was the chief factor, the asphyxia experienced at operation may have contributed to death in the above case Asphyxia at and after operation was probably a material factor in the early death of *Case B 34*, in whom the peritonitis was early and blood volume should have been adequate for recovery

Case B.34 received a penetrating wound of the left side of the abdomen through which the intestines protruded There was a small perforation in the jejunum and an almost complete severance of the ileum

Seen at 11 hr after injury, following the transfusion of a quarter of a bottle of blood, he was pale and cold, his blood pressure was 130/90 and his pulse rate 112

Operation began at 11½ hr, lasted 2 hr, and consisted of laparotomy, suture of the jejunum, end-to-end anastomosis of the ileum and closure Two bottles of blood were transfused

Anaesthesia was begun with 'Pentothal', followed by bilateral intercostal and splanchnic block (95 ml 1 per cent procaine) As this failed to relax the abdominal muscles, anaesthesia was continued with open ether and oxygen The patient was kept in the head-down position throughout

★After the injection of procaine the blood pressure fell to 80/60 The patient vomited and probably inhaled some vomit, some respiratory obstruction followed and per-

sisted throughout operation Injection of 1 ml "Veritol" raised the blood pressure temporarily to 150/85 ★

During the abdominal operation the blood pressure fell to 70/60 and the pulse rate remained about 160 The blood pressure did not rise when the abdomen was closed, but intravenous injection of 85 ml 50 per cent glucose raised it to 95/50

★At this point an attempt was made to intubate the trachea and use suction to relieve obstruction, it failed, and provoked laryngeal spasm with cyanosis and a rise of blood pressure to 160/80, the pulse rate slowed to 140 Artificial respiration was carried out A few minutes later intubation by laryngoscopy succeeded, vomit was seen in the pharynx and removed, the trachea seemed clear A stomach tube was passed but less than 30 ml stomach contents was withdrawn Then, 1½ hr after operation, the blood pressure was 85/60 and the pulse rate 168, the extremities were warm and the veins relaxed, cyanosis persisted The patient was still unconscious He was kept in the head down position and oxygen was administered

At 2½ hr after operation a quarter of the third bottle of blood had been transfused, the blood pressure was 90/65, the pulse rate 104, the lips were still a little cyanosed, the extremities warm and the veins relaxed Blood volume was measured and found to be 85 per cent normal, haemoglobin was 109 per cent During the ½ hr required for the injection of dye and the withdrawal of blood samples (18 ml blood withdrawn in all) transfusion was slowed and only a few ml entered the vein Ten minutes after the last sample was taken the blood pressure had fallen to 50/? and the pulse rate was 168, the extremities were cold and the respirations gasping Transfusion was speeded up and the remainder of the third bottle and one bottle of serum were given over ¾ hr, the blood pressure then was 90–100/60 and the pulse rate 156, the extremities were still cool and the skin a little cyanosed

The patient was then placed in the horizontal position, the blood pressure fell and remained about 75/60 Transfusion was continued slowly with plasma

At 4½ hr the patient was still unconscious He was lying supine with the head turned to one side so that the ends of the stomach and endotracheal tubes were over the side of the bed He seemed to breathe freely The blood pressure was 85–95/60–75 and the pulse rate 172, the radial pulse was wider than it had been and the extremities were warm His condition was unchanged ½ hr later

When next seen, at 6½ hr, he had just died ★ He was lying supine with the tubes in position The head and upper parts of the body were deeply cyanosed and, as the observer watched, the cyanosis faded in patches to leave pale areas The skin was hot, axillary temperature 104 4 F (40 2° C) About 200 ml of plasma had entered the vein The orderly reported that about 5 min previously the patient had pulled his head back so that the ends of the tubes were in the bed and that stomach contents were draining from the stomach tube He readjusted the head Death was unexpected and seemed possibly due to the airway having become obstructed

★Necropsy, 3 hr after death, gave evidence of respiratory obstruction ★ The head, neck and shoulders were deeply cyanosed, there were petechiae in the pericardium and on the lung surfaces, specially between the lobes The trachea contained a considerable amount of frothy vomit and its mucous membrane was deeply congested There was blood stained fluid in the bronchi and both lungs were deeply congested and wet but contained some air Each pleura contained about 400 ml fluid The abdominal cavity contained 400 ml blood stained fluid and there was oedema of the mesentery and of the perirenal tissues The stomach and small gut were distended and reddened and there were patches of fibrinous exudate on their surface The stomach and oesophagus contained undigested food Histological examination showed intense congestion of the lung vessels and extensive haemorrhages into the alveoli A few fat emboli were found in the lungs but none in the kidneys or brain

In two patients who died in circulatory failure 21 and 30 hr after operation, post-mortem evidence suggests that death was due at least in part to broncho-pneumonia Blood volume and blood loss are unknown for both cases

Case B 17 Seen at 36 hr, he looked relatively fit, but his pulse rate was 152, plasma transfusion was begun Operation at 36½ hr revealed six holes in the reddened and sticky small intestine, these were repaired Hypotension developed and persisted (p 147)

Transfusion was continued slowly after operation two bottles of blood were followed by two of plasma and one of glucose saline

Two hours after operation, when he had recovered from the anaesthetic, the blood pressure had risen to 90 60 and the pulse rate was 160, the face colour was good and the extremities were warm Gastric suction was started and from 9 hr after operation morphine ¼ gr was given four hourly (1 gr in all)

At 11 hr the blood pressure, pulse rate and face colour remained unchanged He was restless and stuporous and at times delirious Later in the day the axillary temperature rose to 105 F (40 5 C.), he sweated profusely and became unconscious, his respirations became periodic and his blood pressure fell He died 21 hr after operation (58 hr after injury)

Necropsy, 14 hr after death, revealed thin blood stained fluid in the abdomen and the coils of intestine matted together by fibrinous exudate, but no pus Both lungs were congested and oedematous, particularly the lower lobes Histological examination showed moderately severe bronchopneumonia, in parts confluent A few fat emboli were found in the lungs, but none in the brain or kidneys

Case B 55 received small wounds of the right lower chest (non penetrating) right thigh and right buttock (penetrating the abdomen) Operation revealed some thin blood stained fluid in the abdomen, the small intestine was distended and covered with flakes of fibrin, and there were two perforations of the ascending colon

Seen at 30 hr, he had been transfused with four bottles of plasma (begun at 16 hr) and had received morphine ¼ gr He was drowsy, a little flushed and sweating, his extremities were warm, his blood pressure was 115 50 and his pulse rate 112

Operation, begun 32 hr after injury under nitrous oxide oxygen and ether, lasted 2½ hr and consisted of laparotomy, colostomy of the ascending colon and closure with drainage About 500 ml blood were lost, one bottle of blood and one of plasma were transfused

During operation the blood pressure gradually fell to 75/50 and the pulse rate increased to 160 With closure of the abdomen the blood pressure rose to 95 65, but fell to 85/70 when the anaesthetic was withdrawn

After operation three bottles of plasma were transfused and followed by one bottle of glucose saline

By 1 hr after operation he was conscious but drowsy, warm and sweating with a blood pressure of 100 65 and a pulse rate of 160

By 14 hr he was rational, restless and a little cyanosed, his blood pressure was 80 55 his pulse rate 130 and his respiration rate 28 He remained restless and the blood pressure did not rise An attempt was made to measure the blood volume but the veins were difficult to find and no blood could be withdrawn from them He died 30 hr after operation (64 hr after injury)

Necropsy, 7 hr after death revealed a generalized plastic peritonitis and gangrene of the colostomy Both lungs were congested and oedematous, particularly the lower lobes Histological examination of the lungs revealed many areas of haemorrhagic bronchopneumonia A moderate number of fat emboli were found in the lungs and a few in the brain and kidneys

Remarks

Certain findings, similar to those in patients with injuries to the limbs, are clear

(*a*) The chief and dangerous illness in the early post-operation period is again circulatory

(*b*) Its pattern is hypotension associated with vasoconstriction and tachycardia

(*c*) It is seen mainly in those who have lost much blood before and sometimes during operation, and is commonly associated with a blood volume in the region of 70 per cent or less of the predicted normal

(*d*) The treatment is adequate transfusion before, during and after operation

(*e*) Circulatory failure can also be brought about by developing infection, even though little blood has been lost and the blood volume remains well above the critical level, in this case the circulatory pattern is hypotension associated with a greater tachycardia but less vasoconstriction than is usual with haemorrhage, it may not respond even to large transfusions

(*f*) A few patients have shown periods of low blood pressure with cutaneous vasodilatation although the blood volume was adequate and infection was not obvious, this pattern is not understood These patients recovered, some with and some without further transfusion

It is also clear that the first 24 hr after operation is a period of great danger in those suffering from abdominal injuries and calls for as great attention and as skilful handling as any other period

LATE POST-OPERATION PERIOD

Attention is confined to 57 patients, all subjected to laparotomy, in whom no evidence of peritoneal infection was found at operation and all of whom entered the late post-operation stage with the circulation well restored Thirty-five had suffered an intraperitoneal perforation of the intestine, the chest had been penetrated in eight cases

Observations on the late course of these 57 patients are incomplete For the most part, we did little more than see them daily for the first few days after operation and then at irregular intervals Their general condition and circulatory state were noted and also such details of their fluid intake and output and other treatment as were given in the ward records The presence of bandages made a full examination of the abdomen and chest impracticable Samples of blood and urine from most were examined, and in a number blood volume was measured In only a few of the fatal cases was the final stage observed

These observations showed that only a few patients, mainly among those without an intraperitoneal perforation of the gut, progressed steadily towards recovery and developed no obvious complication before they were transferred to Base, that many cases continued to be ill, and that illness at this stage was not primarily circulatory in origin but arose mainly from three factors (1) disturbances of salt and water metabolism, (2) infection and (3) renal failure

Disturbances of Salt and Water Metabolism

Almost all the patients with an intra-peritoneal perforation of the intestine and over half of those without such a lesion were treated by continuous gastric suction and intravenous salines for at least two days after operation The

saline used was 0 3 per cent sodium chloride and 5 per cent glucose, to which a mixture of 4 per cent sodium citrate and 4 per cent sodium bicarbonate was added when the patient was receiving sulphadiazine Patients were encouraged to drink but no food was given As a result, some of them became dehydrated and salt-deficient, and in others the loss of salt together with the administration of alkali brought about alkalosis We suspected that these metabolic disturbances played a great part in the illness after operation and favoured the development of infection and possibly also of renal disturbance Further discussion will be found in Part IV, Section G, p 295

Infections

A large number of patients developed an infection, and a high proportion (15 cases) died mainly for this reason. The course and outcome were worse in those with an intraperitoneal perforation of the intestine than in others, probably because of the contamination of the peritoneum by the intestinal flora

Pulmonary Infections

In the great majority, at least four out of five, the infection was pulmonary Usually this was not more than the so-called "post-operation chest" not uncommonly seen after abdominal operations in civilian practice It was shown by the development about 48 hr after operation of a cough with sputum, low fever and adventitious signs in the lungs In most instances these signs subsided after several days, in a few, however, there was evidence of persisting lung trouble when they were transferred to Base 10 to 14 days after operation. In a few, all with an intraperitoneal perforation, the lung condition progressed to become a more evident pneumonia (*Cases B* 49, 77, 76 and 51), empyema developed in one other (*Case B* 61) Three of those developing pneumonia had inhaled vomit at operation and two of them died

Case B 76 received wounds of both legs and a small wound near the umbilicus It was doubtful whether the abdomen had been penetrated, but operation revealed three tears in the upper jejunum, one in the mid transverse colon and one in the stomach.

Until operation his condition is said to have been good, he was not transfused

★Operation on the leg wounds was begun at 4½ hr under "Pentothal (1 g.) and had lasted 15 min. when, while the surgeon was examining the abdomen before deciding on laparotomy, the patient vomited and inhaled the vomit. Respirations ceased and he became deeply cyanosed.★ Clearing the air passages and restoring respiration delayed the remainder of the operation about 1½ hr Laparotomy, exploration, suture of the gut and colostomy occupied another hour under ether (Oxford vaporizer and endotracheal tube) He was not transfused

★For some hours after operation he remained cyanosed and his respirations were moist, deep and 40 per minute ★ The blood pressure remained at normal levels but showed a respiratory variation of 10 to 20 mm Hg Oxygen was administered by mask and glucose saline begun intravenously By the time he recovered consciousness 11 hr after operation, cyanosis had disappeared and the respirations had slowed and quietened The blood volume was measured and found to be 93 per cent normal *He passed urine well.*

★Improvement was not long maintained Signs of respiratory embarrassment returned By the fourth day after operation he was dyspnoeic, with stertorous

respirations and marked cyanosis The blood pressure was still normal He was not followed further in detail and died on the seventh day after operation

Necropsy, 8 hr after death, revealed a right-sided fibrinous pleurisy and widespread bronchopneumonia of both lungs ★ There was only a slight peritonitis localized around the colostomy The spleen was soft and grey Histological examination of the lungs showed a few structures resembling miliary tubercles in addition to the pneumonia A few fat emboli were found in the lungs, kidneys and brain

Case B 49 was seen ½ hr after injury The blood pressure and pulse rate were normal, and the blood volume was about 80 per cent normal Plasma transfusion was started During operation (which was begun at 1½ hr and consisted of the repair of four holes in the jejunum and of two tears in the mesentery) the blood pressure was low and the pulse rate slow ★At the end the patient vomited and inhaled vomit, and cyanosis and hypertension ensued for a time (p 138) ★

After operation, treatment with sulphadiazine and penicillin, gastric suction and intravenous glucose and alkali were begun and continued almost till death

★He improved for a time but soon developed signs of a pulmonary complication, and peritonitis was also suspected ★ Fluids were not properly regulated and he became dehydrated, lost much chloride, and towards the end developed alkalosis (For further details see Part IV, Section G, p 295)

By the sixth day he was thin, with sunken eyes and cheeks and a dry, brown tongue, and his abdomen was a little distended His blood pressure was still normal, 120/90 His lips were cyanosed and respirations shallow and rapid (36 per minute)

On the seventh day he was mentally deranged and extremely restless Respirations had increased to 50 per minute and blood pressure fallen to 80/60, with constriction of the forearm veins Rapid transfusion of three bottles of plasma and, later, of another bottle of plasma and one of double strength serum, failed to raise the falling blood pressure He died the same day

★Necropsy, 10 hr after death, revealed a right-sided fibrinous pleurisy and widespread confluent bronchopneumonia of both lungs ★ The small intestine was grossly distended from its upper end to within a foot of the caecum, where it was adherent to the parietal peritoneum and kinked There was some plastic peritonitis in the neighbourhood of the laparotomy wound The left ureter was half cut through by the track of the exit wound but was not obviously infected Except for a distinct cerebellar pressure cone, the brain seemed normal No fat emboli were found in lungs, kidneys or brain

Other Infections

In well over half the patients the continuance or renewal of fever and tachycardia, with anorexia and wasting and often with falling haemoglobin and plasma proteins, indicated the development of further infection The site of infection was not always obvious, it was thought mainly to be intra-abdominal In over a third the infection declared itself as an overt sepsis of the operation or other wounds Gaping of the septic laparotomy wound necessitated a second operation for closure in six patients

In most instances the patients' general condition permitted their transfer to Base Nine, however, died, seven of them had suffered an intraperitoneal and two an extraperitoneal perforation of the intestine Necropsy revealed infection of abdomen and chest in all

In three cases the abdominal sepsis was localized

Case B 24 (pp 126, 136 and 156) died on the fourteenth day A large pararectal abscess was found communicating with the rectum and the heavily infected buttock wound but was shut off from the abdominal cavity by matted coils of gut The abscess

contained a swab Old adhesions fixed both lungs to the chest wall, there was widespread bronchopneumonia of the left lower lobe and smaller areas of pneumonia in the right A few fat emboli were found in lungs, kidney and brain

Case B 30 (pp 130 and 158) died suddenly on the seventeenth day from a large pulmonary embolus There was a large inflammatory mass with pockets of pus in the left hypochondrium beneath the infected laparotomy wound, formed by the matting together of the jejunum, colon, stomach, liver and spleen The left pleura (penetrated at injury) contained 500 ml fibrino purulent fluid, the left lung was completely collapsed The base of the right lower lobe was collapsed and contained foci of bronchopneumonia A few fat emboli were found in the lungs but none in the kidneys or brain

Case B 22 died on the eighth day The ascending colon was gangrenous, there was extensive retro-peritoneal infection behind the colon Both lungs were oedematous and their bases solid No histological examination was made

In four patients there was a generalized purulent peritonitis In two this was associated with extensive bilateral bronchopneumonia (*Case B* 67, died tenth day, *Case B* 28, died ninth day (p 142)) In *Case B* 64 (died eighteenth day) there was a left-sided fibrinous pleurisy and some moderate oedema of of the lungs In *Case B* 68 (died eighth day) the only abnormality in the lungs was a small area of collapse with pneumonic foci at the left lower lobe base

In the remaining two cases, who both died on the fourth day, the peritonitis was less advanced, with fibrin formation but no pus

In *Case B* 52 there was little functioning lung tissue, there was bilateral fibrinous pleurisy with complete collapse of both lower lobes and widespread broncho pneumonia He died suddenly after vomiting and inhaling vomit

In *Case B* 38 an apparently mild peritonitis was associated with gross oedema of the whole body and bilateral bronchopneumonia (p 146)

An unsutured tear of the large gut provided an obvious source for the abdominal infection in five cases (*Cases B* 22, 24, 28, 64, and 68)

It seems from this brief description that infection provides a sufficient explanation for the death of most of these patients, though life was terminated by asphyxia in *Case B* 52 and by a pulmonary embolus in *Case B* 30 In *Case B* 38, however, the relatively early peritonitis can hardly account for death on the fourth day, and the clinical course indicates that it was due to gross alkalosis (p 305) Disturbances of the salt and water metabolism contributed materially to the illness and death of a number of other cases (p 304)

Renal Failure

Four other patients died, not from infection but from renal failure Three had suffered unilateral nephrectomy at operation Only one (*Case B* 32) was followed throughout, two others (*Cases B* 16 and 74) were seen only after operation, when renal failure had already developed, we are indebted to Major G C Rob, R A M C, for the details of the fourth (*Case B* 11)

The cause of the renal failure is obscure The clinical data suggested that in *Case B* 11 it resulted from ischaemia during the long period of low blood pressure arising from haemorrhage and inadequate transfusion, but it

is doubtful whether this could have caused the almost total necrosis of the remaining kidney that was found at necropsy

Case B 11 received a small wound of the muscles of the right side of the back The Regimental Medical Officer who saw him 15 min later thought the wound involved the muscles only and retained the patient with the Unit

*About 2 hr later he was again called to the patient, who was then pulseless, and slow plasma transfusion was begun At 15 hr, when two bottles of plasma had been given, the radial pulse was just palpable, a third bottle of plasma was started and the patient sent to hospital During the journey the transfusion ceased to enter the vein after a quarter of a bottle had been given

Seen at 19½ hr, the patient was pulseless and his blood pressure unmeasurable, the heart rate was about 170 He was comatose, his skin white and cold, his veins were much constricted (it was hot weather) and his respirations periodic Rapid blood transfusion produced dramatic improvement, after two bottles of blood in 15 min the blood pressure was 80/40 and the pulse rate 120, the respirations were regular at 22 per minute The patient was mentally alert and talkative, he was still pale and his fingers were cold, though the skin generally was warm * The blood transfusion caused no reaction

Operation, begun at 19¾ hr, lasted ½ hr under "Pentothal", chloroform and ether Exploration revealed a very large haematoma (about three pints of blood) around the right kidney, whose pedicle was severed, the peritoneal cavity contained at least a pint of blood No other lesion was found and the kidney was excised A third bottle of blood was transfused during operation, at the end of which the patient was flushed and sweating, with a blood pressure of 90/40 and a pulse rate of 100

He was treated with glucose saline and alkalis and sulphadiazine intravenously *For three days he seemed well, but passed no urine By the seventh day he showed the full picture of uraemia, with a blood pressure of 140/100 Venesection of one pint of blood and the administration of magnesium sulphate by rectum produced no improvement, and he died on the eighth day *

At necropsy, 20 min after death, only the urinary tract was examined The left kidney was pale and soft and showed small haemorrhages under the capsule and in the pelvis The ureters, bladder and urethra were normal

Captain R J Shaw Dunn, R A M C, examined the kidney and reported that the naked eye and microscopic appearances indicated almost total necrosis In a few sites active hyperplasia of the tubular epithelium was incipient, no cellular reaction was seen apart from this Haemorrhage was conspicuously absent, only a few tubules (chiefly Henle s loops) contained blood and the glomeruli were small and shrunken There was a little subcapsular haemorrhage

In the three other cases, although blood loss was considerable, more transfusion was given and no long period of low blood pressure was suffered The data suggest that in all three renal failure may have been due to *mismatched* blood transfusion The evidence for this is the occurrence of haemolysis following blood transfusion in *Case B* 32 and the histological examination of the kidney in *Cases B* 16 and 74 In *Case B* 74, moreover, blood transfusion was excessive, and after operation this case displayed the signs of both cardiac and renal failure Remarks on the effects of alkalosis and salt loss on kidney function will be found in Part IV, Section G

Case B 32 received a through and through wound of the abdomen with perforation of the stomach and pancreas and severance of the left renal pedicle

Twenty minutes after wounding he was pale and cold, with a blood pressure of ? 50/? and a pulse rate of 128 Blood transfusion was begun at ¾ hr, and at 2½ hr, when one bottle was ended, the blood pressure was 90/60 and the pulse rate 96, he

was pale, thirsty and nauseated. A bottle of plasma was transfused and the blood volume was found to be 72 per cent normal, indicating a blood loss by haemorrhage of 45 per cent of the original blood The icteric index of the blood was 20 haemolysis was negligible and the blood urea was 52 mg per 100 ml At 4½ hr, when two more bottles of plasma (the second and third) and half the second bottle of blood had been given, and when the blood pressure was 116/45 and the pulse rate 112, operation was begun.

Operation, under 'Pentothal", cyclopropane, ether and oxygen, lasted about 2 hr and consisted of laparotomy, exploration, suture of the stomach and left nephrectomy The peritoneum was stitched over the hole in the pancreas During operation the blood pressure fell to 80/40 but with closure of the abdomen it rose to 120/40 Bronchoscopy immediately after operation, by which a little fluid was removed from the right bronchus, temporarily lowered the blood pressure to 70/45 During operation one and a half bottles of blood (the second and third) were transfused and the fourth bottle of plasma was begun *A blood sample at the end of blood transfusion showed that the icteric index had risen to 60

The blood volume was measured again 15 hr after operation and found to be 85 per cent normal The icteric index was then 250 and there was obvious haemolysis (40 mg haemoglobin per 100 ml), the blood urea was 128 mg per 100 ml *

He was treated with gastric suction for two days and given glucose saline and alkalis intravenously and penicillin almost till death

*By 39 hr after operation he was slightly jaundiced, he had passed only 30 ml urine and a further 120 ml was obtained by catheter His blood pressure was 145/80 and his pulse rate 128 The blood urea had risen to 216, but the haemolysis had decreased and the icteric index fallen to 60 In the next two days only 20 ml urine was obtained and the blood urea rose to 384 mg per 100 ml, pulmonary oedema developed with orthopnoea, cyanosis, coarse rales all over the chest and a blood-stained purulent sputum. He died 98 hr after operation *

Necropsy, 10 hr after death, revealed no signs of peritonitis The peritoneum contained about 1,500 ml blood-stained fluid and there was blood staining and extravasation of blood along the mesenteric attachment of the whole of the small intestine and ascending colon The tail of the pancreas was necrotic and disorganized and there was some surrounding fat necrosis The right kidney was a little swollen and pouted on section, its cortex was pale There were scattered petechial haemorrhages in the pelvis of the kidney and along the ureter The left pleura contained 200 ml blood stained fluid, the right 50 ml There was bruising of the left costophrenic angle and of the upper surface of the diaphragm Both lungs were grossly oedematous

Histological examination of the kidney showed much post-mortem change, many tubules seemed much dilated, no pigment debris was seen in the tubules No fat emboli were found in lungs kidney or brain

Case B 16 received a grenade wound of the right lower chest The missile did not penetrate the chest but tore the liver extraperitoneally and the right kidney, there was a large retroperitoneal haematoma

Before operation his condition was said to be good, the face was well coloured, the extremities were warm and the veins relaxed He was not transfused

Operation, whose duration is unknown, was begun at 11 hr under cyclonal sodium and ether, and consisted of laparotomy, exploration, right nephrectomy and closure with drainage through the loin During operation he became pulseless and sweated, the blood pressure, taken for the first time, was 150/90 and the pulse rate 120, the veins were grossly constricted Three bottles of blood were transfused and towards the end of operation the face colour was again good, the veins were relaxed, the blood pressure was 130/? and the pulse rate 100

After recovery from the anaesthetic, glucose saline infusion and gastric suction were begun and continued for three days In that time he was given 15 bottles of saline and also an unknown amount of alkali and 21 g sulphathiazole On the fourth day about 500 ml blood was withdrawn from the right chest His general condition was

improving and he was passing urine well (40 oz during the fourth day) On the fifth day he was not so well and mentally disoriented, 20 oz urine was passed

*On the sixth day after operation he was quiet and drowsy, but mentally clear and very thirsty, his tongue was dry and brown Respirations, 14 per minute, were deep, the blood pressure was 180/100 and the pulse rate 108 The right chest was dull and the apex beat displaced to the left Jugular venous pressure was not raised, slight lumbar and sacral oedema was present The haemoglobin was 46 per cent and the blood urea about 650 mg per 100 ml (the exact figure is uncertain but was very high), the plasma was very jaundiced He passed 22 oz urine during the day The urine was acid, sp gr 1016, and contained some protein but no red cells, acetone, or bile Sodium sulphate was given intravenously

During the seventh day he became restless and disoriented, his respirations continued to be deep for a time and then became gasping He died towards the end of the day *

Necropsy, 15 hr after death, revealed no peritonitis The left kidney was normal in size and pouted a little on section, and the cut surface was a little pale There was haemorrhage and necrosis around the tear through the liver The other abdominal organs, heart and brain seemed normal The right pleura was filled with brownish fluid and fibrin clot and there was no obvious injury to the pleura The right lung was completely collapsed, and the left congested, oedematous, and stuck by old adhesions to the pleura

*Histological examination of the kidney showed that the glomeruli and afferent arterioles were normal, the convoluted tubules were distended and contained eosinophil granular debris like that seen after incompatible blood transfusion * A few fat emboli were found in the lungs but none in the kidney or brain

Case B 74 received a small wound of the upper abdomen (no exit wound) with three tears in the duodenum, one in its mesentery, three in the upper jejunum and two in the transverse colon

At 1½ hr after injury he was pale, his blood pressure was 110/70 and his pulse rate 80 Two bottles of blood were transfused over 2 hr, his blood pressure then became 104/70, his pulse rate 104

Operation, begun at 4 hr, lasted 4½ hr and consisted of laparotomy, exploration, suture of the intestine and colostomy The abdominal cavity contained about two litres of blood, and a large retroperitoneal haematoma lay behind the caecum and ascending colon. Anaesthesia, induced with nitrous oxide, was maintained with ether and oxygen through Heidbrink s apparatus, administration was smooth

During operation nine bottles of blood (the third to the eleventh) were transfused The twelfth was begun towards the end of operation and continued slowly afterwards The surgeon remarked that throughout operation bleeding was profuse from all areas, even from skin and muscle, and he suspected that the patient had been given too much blood The blood pressure remained about 95/65 and the pulse rate about 88 The patient s face became deeply coloured

At 10 hr after operation glucose saline infusion and gastric suction were begun and continued for three days, in which time 21 bottles of saline were given The amount of fluid withdrawn by suction is unknown Sulphadiazine and alkali, also in unknown amounts, were given by vein

*During these three days there was a low fever, and tachycardia persisted The skin, highly coloured after operation, became cyanosed and jaundiced, oedema developed and the blood pressure ro e to 150/110 No urine was passed Small amounts were withdrawn by catheter twice daily and contained much blood and many casts

Four days after operation he was quiet but disoriented and resented examination His muscles twitched The abdomen was not distended The veins of the neck were engorged to a height of at least 5½ cm and the skin was plum-coloured and jaundiced The face was puffy and both arms a little oedematous, while the lower trunk, thighs, scrotum and legs were all grossly oedematous The blood pressure was 150/100 and

the pulse rate 104, while the respirations were deep, and 20 per minute Haemoglobin was 91 per cent and blood urea about 450 mg per 100 ml (exact figure uncertain but very high) He was thought to show cardiac and renal failure ★

Over a litre of blood was withdrawn from a vein and 4 2 per cent sodium sulphate was given intravenously

★During the next 48 hr the high skin colour, cyanosis, venous congestion and oedema subsided, his face became a little pale The blood pressure and blood urea remained high No urine was passed and small quantities (less than 50 ml) were removed by catheter twice daily it was alkaline, with a specific gravity of 1016 and still contained blood ★

He remained disoriented, and finally became unconscious and died on the seventh day after injury

Necropsy, 9 hr after death, revealed no subcutaneous oedema and no evidence of peritonitis or of obstruction to the bowel The intestinal sutures were sound The spleen was enlarged and rubbery and the liver showed patchy fatty changes Both kidneys were a little swollen and congested, both ureters were patent The bladder was normal except for a small haematoma and a patch of oedema at the base The heart was normal except for slight dilatation of the right side, and both lungs were congested and oedematous

★Histological examination of the kidneys showed eosinophil debris in almost all the Bowman s capsules and the convoluted tubules A large proportion of the collecting tubules contained reddish brown debris like that seen after incompatible blood transfusion No fat emboli were found in lungs, kidneys or brain ★

Other cases suggest that infection also may play a part in the production of renal failure, although the data are insufficient to exclude other factors such as fluid and salt loss For example

Case B 57 (pp 150 and 164), the sole survivor of the 12 patients who had initial peritonitis, suffered only a short period of hypotension and was transfused with only one bottle of blood before operation, without haemolysis occurring For three days after operation he was on suction and salines) oliguria lasted into the fourth day, while a rise of blood urea to 60–80 mg per 100 ml persisted to the ninth day) urea clearance was depressed to 45 per cent normal on the seventh day, rising to 72 per cent on the eleventh day He was doing well when last seen on the twenty first day

One further patient, not in this series, is of interest in this connection For the correction of secondary anaemia he was given a transfusion of about 70 ml blood which proved to have been heavily infected with a coliform bacillus and which produced a pronounced fall of blood pressure and anuria Recovery of the blood pressure and renal function followed further transfusion of plasma and fresh blood

Case B R underwent an operation for the removal of a bullet lodged between the 11th and 12th ribs The bullet had been left there at a previous operation for an abdominal injury 25 days earlier The blood pressure had been maintained throughout

While he was recovering from the anaesthetic (Pentothal and cyclopropane) and just before transfusion began, the blood pressure was 115/70, the pulse rate 88 and the respirations 20, he was warm and of a good colour The haemoglobin content of the venous blood was 65 per cent and the plasma proteins were 7 0 g per cent

★After 14 min of slow transfusion he was awake and shivering, and showed goose skin the radial pulse was difficult to feel and the forearm veins were no longer visible, the blood pressure was 120/85, the pulse rate 128 and the respirations 28 Since the rigors continued, the transfusion was stopped when about 70 ml blood had been given Half an hour later he was sleeping, with a blood pressure of 100/50 and a pulse rate of 136, his extremities were cool and his respirations 24

the study of abdominal wounds shows that, as in limb wounds, the recognition, assessment and treatment of blood loss by haemorrhage are of prime importance. But the visible injuries give little or no help in assessing the extent of loss, which is largely concealed until operation; so that assessment must usually be based on a study of the general circulatory state, which is determined by blood volume. The rules already found to apply in the case of limb injuries can be used here too. So long as blood volume remains above the critical level of 70 per cent normal, the blood pressure remains normal; when it falls below this level the blood pressure is low. When the blood volume is normal or nearly so, as a rule the pulse rate is normal, the face is well coloured, and the extremities are warm. When the blood volume is below 80 per cent normal, a combination of tachycardia, pallor and cold extremities is the rule. Marked circulatory failure again indicates gross reduction in blood volume and the need for immediate and rapid transfusion.

The relation between circulatory state and blood volume may be disturbed if the patients have already been transfused: tachycardia, pallor and cold extremities are then the rule irrespective of the level of the blood pressure or blood volume.

If patients are seen later than about eight hours after injury the possibility of infection has to be borne in mind. Infection may, on the one hand, cause plasma loss and decrease a blood volume already reduced by haemorrhage or, on the other, poison the circulatory control and lead to hypotension even when the blood volume is well above the critical level or even normal. Hypotension caused by infection seems to be associated with greater tachycardia but less vasoconstriction than that caused by haemorrhage. Gross plasma loss may be recognized by finding haemoglobin or haematocrit values above those normal for venous blood, but is uncommon.

Because the full extent of the wound cannot be seen and because of the possible effects of infection, the assessment of blood loss and blood volume is less reliable in abdominal than in limb cases. However, in the majority of cases blood loss is not gross, being no more than 30 per cent of the total blood and often considerably less. Usually the evidence derived from examination of the circulatory state provides a sufficient basis for determining treatment before operation. In difficult cases, measurement of the blood volume is of great value.

Abdominal, like limb cases, do best at and soon after operation when blood volume is maintained well above the critical level; 90 per cent normal again seems a safe level for the beginning of operation. Therefore the same rules apply for transfusion before operation as in the case of limb injury.

In patients seen soon after injury, in whom loss of whole blood is the factor reducing the blood volume, the fluid transfused should be blood. In those seen later, when fluid may have been lost from the blood and a rise in the red cell content may be increasing the difficulty of circulation, transfusion of plasma or blood and plasma seems preferable. In any case the course of transfusion should be guided by following the changes in the blood (haemoglobin or haematocrit and plasma proteins). Experience is too limited to permit the statement of more precise rules.

How to restore circulation in those unusual cases in which transfusion fails to do so, whether because of infection or for some other reason, is not known

The only other modification of the pre-operation therapeutic measures referred to in Part I is in the administration of fluid by mouth this should be withheld and the patient allowed only to moisten his mouth

Early operation is urgent in all cases and should be undertaken as soon as transfusion is judged adequate to replace blood loss, whether or not the blood pressure has been restored

At operation, transfusion should be continued slowly so that it may be speeded if required No particular anaesthetic agent has been found to be preferable, but skilful administration is of the greatest importance

All cases require watching with the greatest care for the first 24 hr after operation in case further transfusion should be required The level of the blood pressure is the best clinical guide here, and the measurement of blood volume gives a clear indication of the amount of transfusion required

In the late post-operation period the possibilities of a developing infection, of dehydration, of salt loss and of alkalosis must be constantly borne in mind Particular attention must be paid to the fluid intake and output, the chloride content of the urine, and the chloride and bicarbonate content of the plasma Further transfusion may also be required for the correction of anaemia and hypoproteinaemia For anaemia, fresh rather than stored blood is preferred

It is clear that much remains to be learned

PART III

DISCUSSION

We now discuss our findings in the various stages of illness in relation to the observations of others, confining our attention to observations on man. Views about "shock" have been much influenced by conclusions drawn from animal experiment; but until there is general agreement about what is meant by "shock" in man and until the clinical picture is defined clearly it is impossible to be certain if the same state has been reproduced in the animal, especially since the animal has usually been under the influence of an anaesthetic. Moreover, the recent advances in diagnosis and treatment of the general effects of injury have been gained by observations on man rather than on animals.

Initial State

CONFUSION ABOUT "SHOCK"

The confusion arising from the lack of a generally accepted and precise clinical definition of "shock", and from lack of illustration to show what condition is referred to by any particular writer, has been mentioned briefly in the introduction. The matter requires further discussion.

The term "wound shock" was introduced by Cowell (1919), "to avoid the confusion which arises, even among army medical officers, if the word 'shock' alone is used". He also first separated wound shock into primary and secondary types.

Primary Wound Shock

According to Cowell "wound shock may supervene early on. That is, the man suddenly becomes pale, clammy and pulseless; and a low blood pressure may be found as soon as it is possible to make a reading 15 to 20 min. after the man has been hit. To this group of symptoms with hypotension the name *primary wound shock* is given." He quotes briefly several cases to illustrate early wound shock. It is to be noted that of the six cases in which the pulse is mentioned, two are pulseless, and the pulse rate in the others is given as 68, 80, 84, and 96, also that one patient seen 2 hr. after wounding (severe buttock wound penetrating the abdomen) was so restless that he had to be held on the stretcher by two orderlies. The patient with primary wound shock might die soon after injury, or recover speedily, or pass into the state of secondary shock. Although Cowell recognizes that transient hypotension sometimes follows trivial wounds, he later (1922) associates primary wound shock specially with serious wounds. "Where the damage was such that anatomical death must have supervened unless surgical intervention was possible or available, the pressure fell with great rapidity and the symptoms of wound shock were found to have become established as soon as the patient was seen. To this class of case the name *primary shock* is given." He adds that in war surgery it is doubtful if such a state of affairs occurs apart from haemorrhage.

Cannon (1919) modifies Cowell's (1919) account and describes primary wound shock as "dusky pallor, rapid, thready, low-tension pulse, hypotension, sweating, thirst and restlessness" He remarks that it may come on so soon after injury as to be explicable only as the result of nervous action He suggests that Cowell's observation of fainting after slight wounds may perhaps be regarded as a transient state which, in pure shock, is more prolonged He extends (1923) the definition of primary shock to include not only cases with serious wounds in Cowell's sense, but also less severe cases ("merely shot through the hand", "only a bullet wound in the thigh") and even those in which "all the classic symptoms of shock appeared though there had been no gross injury at all" Of the last type of case, he refers to two cited very briefly by Wallace (1919), "One was buried by the explosion of a shell in a cellar, the other was blown up by a buried shell over which he had lighted a fire Both exhibited all the classic symptoms of shock, which lasted over forty-eight hours, in both treatment was of no avail In neither did the post mortem examination show any gross lesion"

Phemister and Livingstone (1934) again modify the clinical picture of primary shock on the basis of observations on a number of surgical cases at operation and on one case of accidental injury They apply the term primary shock to a state of hypotension, bradycardia, pallor and faintness, developing rapidly after injury and brought about by activity of the nervous system They hold that primary and secondary shock should be distinguished by differences of aetiology rather than of time of occurrence

Their case of accidental injury is that of a 54-year old woman admitted 15 min after sustaining numerous contusions of the left half of the body, with fractures of the left clavicle, scapula, second to ninth ribs, tibia and fibula, and emphysema of the left chest wall She was conscious, anxious, restless and in great pain, her blood pressure was 100/64, her respirations were shallow and 30 per minute During the next 45 min, while physical and X-ray examinations were made, her blood pressure declined to 60/40 mm Hg, while her pulse rate ranged from 76 to 70 per minute and her respirations were unchanged She was then transfused with 300 ml. saline and 400 ml blood, 1,200 ml saline were given subcutaneously Her blood pressure rose to 130/70 mm Hg within an hour, and remained elevated despite a stormy convalescence

The authors remark that in this instance of primary shock "the most important cause appeared to be psychic (from the great pain), although haemorrhage and respiratory embarrassment from fractured ribs played a role"

Kekwick, Marriott, Maycock and Whitby (1941), in their study of secondary shock, describe primary wound shock as common among air raid casualties reaching hospital soon after injury

Most are at least frightened and shaken These from primary shock alone [due to psychogenic and neurogenic influences] may exhibit pallor, sweating, feeble pulse and low blood pressure or even be unconscious Differentiation of primary from secondary shock is easy with extremes of injury, when the wounding is of such severity that transfusion is obviously required and delay would be dangerous, or when there are no wounds and transfusion would be both unnecessary and foolish But in intermediate cases differentiation is only possible by allowing a period of observation, the degree to which rest in the recumbent head-low position combined with warmth and morphia produces improvement will depend on how far the symptoms are due to primary shock If

4 who were "moribund on admission to hospital". From the data it is not possible to discover on what grounds the classification was made. Thus in *Class A*, with varied wounds, blood pressure ranges from 45 to 80 and pulse rate from 108 to 160; in *Class D* also with varied wounds, blood pressure ranges from 38 to 86 and pulse rate from 116 to 140. In *Class B* are 5 cases with normal blood pressures (116 to 144) and 2 with normal pulse rates (72 and 76); in *Class C* 2 cases have normal blood pressures (120, 124), both with pulse rates of 88. One of *Class B* (both haemorrhage and shock of moderate degree) is described in greater detail:

> *Pte. N.* Admitted 2¼ hr. after being wounded in both legs by rifle grenade. The patient was very pale and restless on admission, and the radial pulse was not palpable The carotid pulse rate was 95 per minute Temperature below 95° F. Respirations 22. Systolic blood pressure 76 mm. Both legs were severely shattered, the right leg being blown off in the middle third. The left leg showed severe compound fractures of the tibia and fibula in the middle third, with, in addition, mutilation of the ankle-joint and tarsus. The large amount of blood in the dressing and on the stretcher made it evident that haemorrhage was still active. A tourniquet was immediately applied round each thigh, and transfusion with the solution of gum acacia begun at once The blood pressure at the end of the transfusion had risen from 76 mm to 122 mm, and the patient was obviously much better. Double amputation was thereupon performed, which led to a fall in blood pressure to 92 mm Twelve hours later the pressure had risen again to 104, while his pulse rate was 120. The patient made a good recovery, and was sent to the Base eleven days later.

Fraser (1922) also gives the clinical picture of wound shock as seen in soldiers at a Casualty Clearing Station.

> The patient may be described as being in a state of prostration. He is roused with difficulty from what appears to be a condition of mental indifference yet he answers questions clearly and intelligently, if faintly The face is drawn and pale, beads of perspiration stand out on the brow, the eyes are sunken and the cheeks hollow The lips and ears are pallid The body surface is grey in appearance, being cold and clammy to the touch The pulse is rapid and fluttering, and often imperceptible at the wrist ... The general body temperature is low The mouth is parched and the patient complains of thirst.
>
> Shock respiration is of the superficial, rapid type, and is very similar to that with which the clinician is acquainted in toxaemias and after severe haemorrhage The shock victim breathes rapidly. There are occasional deep sighs or gasps, and at intervals there is what can only be described as a quick respiratory 'flutter'.
>
> The characteristic motor disturbance of shock is an increasing motor weakness, which eventually extends into what one may term a general muscular apathy.
>
> One of the most striking evidences of shock is a diminished sensibility to stimulation. The blunting of sensation and the general apathy are features which have been emphasized in all the clinical accounts of the shocked state.
>
> During the progress of a case of shock, there is an increasing tendency to concentration of the blood in the superficial capillaries.

He gives no indication of the picture in the various degrees of shock other than that the intensity of the features varies and offers no case histories to illustrate his description.

Cannon (1923) gives a briefer account which seems to be intermediate between the two strikingly different pictures of Keith and Fraser.

Shock is a general bodily state which occurs after severe injury and which is characterized by a persistent reduced arterial pressure, by a rapid thready pulse, by a pallid or greyish or slightly cyanotic appearance of the skin which is cold and moist with sweat, by thirst, by superficial rapid respiration, and commonly by vomiting and restlessness, by a lessened sensibility and by a somewhat dulled mental state

He quotes two cases from the older literature (1870 and 1895) in support of his description and gives also a very brief account of a soldier wounded in the 1914–18 war in which the only features referred to are the coldness, impalpable pulse and low blood pressure

He remarks later that low blood pressure is probably the central feature, or one of the most essential features, of shock The degree of reduction of pressure may be regarded as a fairly satisfactory index of the degree of shock which is prevailing He repeats Cowell's remark that early observations after wounding reveal no alteration in pulse rate and no lowering of normal blood pressure In the course of a few hours, however, especially through the action of accessory factors, the blood pressure begins to fall, the pulse rate to rise and the other phenomena of shock likewise to become established

Moon (1938) relegates his description of the signs of shock to an appendix to his monograph He prefaces it by remarking that there is complete agreement concerning the signs of shock as set forth by clinical observers

Prostration is evident, the patient is profoundly depressed, weak and restless The pulse is rapid, feeble and of small volume The extremities are cold and the body temperature is low The face is drawn, ashen or livid in colour, anxious in expression and moist with cold sweat The eyes are sunken and surrounded by bluish rings, producing the classical Hippocratic facies Thirst is incessant, but attempts to relieve it are ineffective because of vomiting The fluid vomited is often in excess of that swallowed, and it contains small brown flocculi Perspiration is profuse, and there may be diarrhoea The respiration is shallow and interspersed with deep sighs The blood pressure declines progressively Urination is scanty or suppressed Consciousness is retained until finally there is loss of sensitivity, of responsiveness to stimuli and of reflexes Unconsciousness or coma precedes death

The physician who awaits the development of this clinical picture will seldom treat a case of shock successfully

A grave mistake is made by those who depend upon blood pressure as an indicator of the condition of the circulation A marked decline in pressure never occurs early and often appears only in the terminal stage (This observation applies to shock, not to syncope)

Haemoconcentration is a feature which appears early, is regularly present, which progresses in a degree paralleling that of the circulatory deficiency, and which is detectable by simple means

One cannot understand why a phenomenon which is so common in occurrence, so grave in its import and so easily demonstrated, has not been utilized clinically Experience indicates that haemoconcentration is the earliest detectable sign of shock

He gives no illustrative clinical histories, but it is apparent from the context that the above description is intended to apply to wound shock, which he refers to as traumatic toxaemia The five charts given in the book to illustrate the development of haemoconcentration before the decline of blood pressure relate, one to an animal experiment, one to shock associated with icterus gravis and three to shock associated with abdominal operations

Blalock (1940) prefers to call shock peripheral circulatory failure. He considers that "uncomplicated neurogenic or primary shock usually does not persist very long and rarely presents difficulties in diagnosis and treatment. Not infrequently, however, additional factors lead to the development of secondary or the haematogenic type of shock, and the outlook is more grave." Most of the following remarks apply in particular to the latter type of disturbance.

The *general appearance* of patients with peripheral circulatory failure varies according to the acuteness of onset and the severity of the disorder. When shock develops acutely, the patient is at first weak and apathetic but rational. As the condition progresses the voice becomes distant, responses to questions are delayed, and perception of visual and of auditory stimuli is impaired At a later stage stupor sets in and finally gives way to complete unconsciousness The countenance is drawn, and the temperature of the body declines. The skin—at first pale—becomes dusty [? dusky] and ashen—the colour resembling that of a cadaver or of a patient with argyria Over the flanks, the back, and the other dependent portions a reddish blue mottling can usually be observed against the background of the paler areas. The skin is cold and moist in patients in so-called secondary shock, peripheral vasoconstriction being present. Even in the presence of a marked elevation of internal temperature, the extremities may be cold This syndrome—apathy, ashen cyanosis, and clammy skin—is so characteristic that the diagnosis of shock can often be made at a glance. When peripheral circulatory failure develops more slowly and especially when it occurs as the result of excessive vomiting or severe diarrhoea, the general appearance is different Here the characteristic apathy and stupor may be accompanied by delirium Muscular twitchings are common, and a coarse volitional tremor is often observed The cheeks are hollow, the eyeballs are sunken and soft, and the tongue is shrivelled and parched. The skin is loose and dry; its normal elasticity is lost. When pinched into folds, it tends to retain for a time the abnormal contour.

Aside from the alterations in the mental state, in the general appearance and in the skin, the most characteristic features of peripheral circulatory failure are to be found in the vascular system The radial pulse is rapid, small in volume and "thready". In advanced cases it may be imperceptible. The pulsations of all the peripheral arteries are likewise diminished The *veins* are abnormally empty, are not readily located, and fill only slightly distal to a tourniquet. Venipuncture is unusually difficult, and even when a vein has been entered blood cannot be easily withdrawn.

The *blood pressure* undergoes characteristic alterations, the most constant of which is the reduction in pulse pressure. In the early stages, there is a slight to moderate decline in the systolic level often accompanied by a slight rise in the diastolic value As the condition progresses, both pressures decline—the systolic more than the diastolic. In the advanced stages the decline becomes so pronounced that the blood pressure cannot be measured. . . .

In contrast to the marked changes in the circulation, there is but little modification of *respiration* in patients with peripheral circulatory failure . . . In the early stages the respirations may be somewhat rapid As stupor and finally coma occur, the breathing becomes deeper and slower with an occasional sigh Pronounced irregularity of respiration and gasping with use of the accessory muscles occurs only when the patient becomes moribund.

. . . Patients in shock are usually unable to retain fluids taken by mouth. . . . The urine becomes scanty and fairly high coloured. . . . Haemoconcentration rather than dilution is the more frequent finding in peripheral circulatory failure because of the fact that there is a greater loss of plasma than of red blood cells in most instances of shock. . . .

These findings may be observed under a variety of circumstances, such as following trauma, operations, burns, internal or external haemorrhage, the perforation of a hollow viscus . . ."

Scudder in his monograph on shock (1940) gives no clinical picture of the condition He instances six cases of shock due to trauma alone, four due to trauma complicated with haemorrhage, and four due to haemorrhage alone (gastro-intestinal) The data reported, however, refer chiefly to blood studies and do not provide adequate information about the clinical state Harkins in his 1941 review does not consider diagnosis and deals almost entirely with experimental work on traumatic shock carried out since the end of the first world war

Kekwick *et al* (1941), who briefly report the clinical findings in 24 cases of secondary shock in air raid casualties, do not give a description of the condition But they discuss the features valuable for assessing the degree of shock In general they found that "the blood pressure is the most reliable measureable factor for assessing the severity of secondary shock and that other clinical manifestations are variable and not quantitative" The pulse rate was not always as rapid as is generally assumed nor did it rise in proportion to the fall of the blood pressure Five of their cases had rates of 86, 82, 104, 92 and 70 with systolic blood pressures of 55 mm Hg In the remainder the pulse rate ranged from 110 to 155 and did not appear to bear any constant relation to the blood pressure They emphasize that the mental state was clear and rational Colour changes were common but in no way quantitative, 22 of the 24 patients showed obvious pallor and most had cyanosis of the lips and nails The general temperature of all severe cases was subnormal and their extremities were cold Sweating was present in 15 cases but the amount was by no means related to the degree of shock

Cope (1944) gives a definition of shock which, as he points out, "does not specify any particular symptom, for the first thing the clinician should learn is that there is hardly one symptom of shock which is constant" He quotes Cannon's description with approval but remarks on the omission of a subnormal temperature, which he (Cope) regards as one of the most constant signs, and says that it does not apply to the lesser degrees and that some serious cases depart from the classical picture

> Shock may be indicated by a subnormal temperature with a low blood pressure, although the pulse-rate may be within normal limits Or it may reveal itself by pallor, sweating, subnormal temperature and a small rapid pulse, while the blood pressure may remain approximately normal And there are also cases in which the appearance and mental condition give no indication of the serious state of the circulation which the sphygmomanometer may demonstrate
>
> When a person has sustained injuries which are likely to produce shock one must assume the presence of latent shock even though the general appearances belie this diagnosis The good clinician does not judge the picture by one single part of it

Cournand *et al* (1943) studied a series of civilian patients suffering from various injuries Soon after admission to hospital, the clinical signs and symptoms were evaluated and then various procedures were started to measure cardiac output, blood volume, intravascular pressures, renal glomerular filtration and plasma flow The series of measurements was repeated at intervals and after therapy Few details of the injuries and very few case histories are given The average values for their measurements are related

in the tables and figures to the cases grouped in various degrees of shock. Grouping is made on an unusual basis, for the authors say that "differentiation as to the degrees of shock has been done in the light of all available data, including the extent and time of the injury, clinical manifestations on admission, the laboratory findings, and the subsequent course". How these various elements were combined to assess the degree of shock is not displayed. Evans, Hoover, James and Alm (1944), in their studies on blood volume changes in traumatic shock as seen in civilian casualties, arrange their 142 cases in various grades of shock but again do not explain how the grouping was done, nor do they give case histories. Emerson and Ebert (1945) in their studies on 57 shocked battle casualties do not deal with the diagnosis of shock; only a few case histories are given. Cleghorn and Chute (1945) do not discuss their battle casualties (100 cases) under the term "shock": in fact, they say that the word "shock" should be dropped. "It connotes one thing for one observer, and something else for another. If it doesn't make for recognizable confusion, it creates a deceptive clarity by epitomizing, in one word, a multitude of problems. Its brevity is the source of a false sense of security." They give numerous detailed case histories to illustrate the general effects of injury. Noble and Gregersen (1946b), reporting on the blood volume measurements in the same series (109 cases) as that of Cournand *et al.*, arrange them according to their degree of shock but do not further define the criteria used, nor do they give case histories from which their diagnostic criteria might be inferred.

Comment

These quotations illustrate the chief descriptions of the clinical picture of shock, of the features that are regarded as diagnostically important and of the supporting evidence from observations on man.

Three points are evident:

(1) Though the various descriptions bear a resemblance to each other and have features in common, yet they differ in important details. The descriptions of secondary shock given by Fraser (1922), Cannon (1923), Moon (1938) and Blalock (1945) are more or less alike, but they depart widely from that of Keith (1919a and b). It is in fact difficult to believe that Keith and Fraser, who both describe shock as seen in wounded soldiers at Casualty Clearing Stations during the first world war, are speaking of the same condition.

(2) There is no general agreement as to which of the features commonly mentioned are essential for diagnosis and which are of secondary importance. There is a range of choice from the combinations of symptoms and signs used by Keith (1919a and b), through blood pressure according to Cannon (1923) and haemoconcentration according to Moon (1938), to the vague criteria of Cope (1944).

(3) There is a remarkable lack of adequately detailed case reports to show what kinds of case the authors have in mind to support their general descriptions. The importance of such reports is clear. For example, they would have shown whether or not Fraser (1922), who gives no illustrations, is speaking of the same type of case as Keith (1919a and b), who gives brief descriptions.

It is clear, therefore, that at the beginning of the second world war we had good reason to doubt whether or not our air raid or battle casualties were suffering from shock, or, if we thought they were shocked, whether the shock was secondary or primary Subsequent writings have not removed these doubts The uncertainty makes it hard to understand the remarks made by Cournand *et al* (1943) on the clinical manifestations associated with the various types of wounds Thus we find it difficult to relate to our own experience their statements that "patients with skeletal trauma not in shock had more symptoms and fewer signs, those with severe shock fewer symptoms and more signs" and that "in general the patients with abdominal pathology showed more of the usual clinical signs and symptoms of shock than those with skeletal trauma with a comparable degree of circulatory failure" Again, it prevents the clinician from translating important conclusions into practical terms Thus Noble and Gregersen (1946b), reporting blood volume measurements on Cournand's cases, conclude that "a patient in severe shock from either haemorrhage or trauma has lost approximately 2 litres of blood" This conclusion could be of great practical importance in the treatment of injured patients if it was clear what criteria had been used to recognize "severe shock", especially as Cournand and his colleagues say that these were clinical

Even with the experience of the war years we find it difficult to bring the writings of others into a true perspective But it seems clear that under the term "shock" various clinical syndromes have been described which, though they bear a resemblance to each other, are in fact expressions of different states of illness For example, we never saw the pictures of Fraser (1922), Cannon (1923), Moon (1938) and Blalock (1940) associated with limb injuries, we saw something like them associated with abdominal injuries, but only in patients suffering in addition from infection (peritonitis), dehydration and salt loss It is possible that under the conditions of the first world war Fraser's picture was common in wounded soldiers, we think it more probable that the writer had abdominal injuries in mind, though the context does not make this clear Again, we can now see that Keith's (1919a and b) description applies particularly to young men seen some hours after wounding, it requires considerable modification for other injured men, particularly those in the older age groups and those seen soon after injury

We suspect that Cournand *et al* (1943) adopted their unusual method of assessment because they found that grouping in degrees of shock by clinical means did not correlate well with grouping by blood volume, cardiac output, etc If it is true, as is so often said, that the clinical picture is so characteristic that it can be recognized almost at a glance, there seems to be no reason why these complicated laboratory methods should be required, and conversely, if these are necessary for the satisfactory assessment of the degree of shock, then assessment is not feasible for the clinician at the bedside

We know from our own experience that injured patients cannot on the ill-defined basis of "shock" be separated satisfactorily into groups whose members all have the same prognosis and require the same treatment Such an attempt results in practice in the inclusion among "shocked" cases of

(1) some whose apparent illness is due to loss of blood and (2) some in whom it is due to other causes, such as pain, fright, cold or infection. The relative proportions of (1) and (2) in any group of "shocked" patients will depend on several factors: the type of injury, the circumstances in which the patient is seen (e.g. the time after injury, the temperature of the surrounding air), and on what criteria the individual uses, consciously or unconsciously, in making the diagnosis. We have no assurance, therefore, that cases grouped by one man as "shock" or "no shock" or in a particular degree of "shock" will correspond at all closely in underlying causative factors, or even in symptoms or signs, with those so grouped by another.

The paramount need is for adequate description of wounded patients of different ages and with different injuries, seen under different circumstances and at different stages of their course. Only with this factual basis can we proceed safely to consider classification and interpretation in terms of causative factors.

UNDERLYING MECHANISM OF ILLNESS

Though the view had arisen earlier, Keith (1919b) was the first to show by measuring the blood volume (vital red method) that wound shock is consistently associated with a reduced blood volume and that the degree of reduction bears a definite relationship to the severity of the patient's clinical condition. He concludes that in the majority of his patients (29 wounded soldiers, in 27 of whom blood volume was measured) the primary haemorrhage was sufficient to account for the subsequent reduced blood volume: from the context it seems likely that the primary haemorrhage was not estimated from the plasma volume and haematocrit but from the history of bleeding and the examination of the wounds, etc. But he also concludes, and quotes two cases to show, that "in shock with haemorrhage the actual blood lost cannot always account for the markedly reduced blood volume" (Case J. A.) and that "even without haemorrhage shock may be accompanied by a fall in blood volume" (Case S. S.).

Case J. A, aged 22, was seen 5 hr. after wounding He had a fractured pelvis, but no external injury. His blood pressure was 35/–, his heart rate 80, his respiration rate 24, haemoglobin (venous) 80 per cent and blood volume 55 per cent normal At 12½ hr blood pressure was 60/40, pulse rate 116, respiration rate 24. At 13½ hr. he was given 500 ml 6 per cent gum acacia solution with no physiological response. At 17 hr. he died Necropsy revealed the right internal iliac artery cut and a large extraperitoneal haematoma. The clot was measured as accurately as possible and found to amount to 1,000 ml

Case S S, aged 19, was seen 6 hr. after injury; he had no gross wound, but a few superficial bruises. He was suffering from severe wound shock. Heart rate, blood pressure and respiration rate are not given Six per cent gum acacia solution (6 ml) was given by vein. At 42 hr. he was very restless, with a blood pressure of 105/80, a pulse rate of 128, respiration rate of 28 and haemoglobin (venous) 125 per cent. At 43 hr the heart rate was 106 and the respirations 30 (blood pressure not given). At 46 hr. he died Necropsy showed no gross external or internal haemorrhage; there was a small haemorrhage into pancreas and mesentery. In this case the blood volume was not measured, but the high haemoglobin percentage, particularly after the injection of the gum solution, indicated a reduction of blood volume of at least 25 per cent

He goes on to say that it seems evident that the reduction of blood volume in wound shock is secondary to some still unknown *primary factor* For he says that "in normal individuals, such as a donor for transfusion, the withdrawal of a considerable quantity of blood up to 800 c c is followed by a very rapid return of the blood to its original level" He quotes one instance (Case W G, in his Table 1) to show that not only can the original volume be reached within an hour, but the compensatory dilution may be carried still further and result in an actual increase in the blood volume But he says that this restoration of volume is not found in cases of wound shock In compensated cases, it is true, the blood volume is never below 75 per cent normal and the plasma volume is proportionately larger, being 85 to 90 per cent of the normal, thus giving evidence that the needed fluid is slowly but spontaneously passing into the blood stream In partially compensated cases the total blood volume is only 65 or 75 per cent normal, and the plasma volume between 70 and 80 per cent, while in uncompensated cases the blood volume is below 65 per cent of the normal, frequently between 50 and 60 per cent The lowest plasma volume obtained was 62 per cent and in this case the passage of fluid into the vascular system must have been materially retarded Hence he concludes that "when the loss of blood is excessive or when there is a severe trauma, a shock-like condition follows which is distinguished by a failure of the normal process of rapid restoration of fluid to the vascular system"

Robertson and Bock (1919b) also, from their blood volume studies on wounded men suffering from haemorrhage, concluded that in many instances dilution of the blood occurs very slowly But they thought that the principal reason for the lack of prompt dilution was "an initial marked diminution in the reserve fluid of the tissues and the lack of any subsequent attempt [by the body] to make up this fluid deficiency" In view of later work, it is important to note that Robertson and Bock showed that many of their patients had lost more blood than was commonly supposed Most of their patients were observed late after injury, from one day onwards, but they quote an excellent instance of one seen soon after injury in whom the haemorrhage was initially underestimated and the patient's condition attributed to "shock" We have pieced together the data given in the text and chart of their paper

A civilian, aged 29 years, had both lower legs crushed and partially amputated by a train When he was seen 1 hr later, it could not be ascertained how much he had bled Ear haemoglobin was 94 per cent, vein haemoglobin 88 per cent, blood pressure 65/45, pulse rate 110 The general opinion was that he was suffering from shock

He was put on fluids by rectum shortly after admission, but these were not pushed energetically enough At about 3 hr, when blood pressure was 70/40 and pulse rate 120, operation (double amputation through the lower third of both thighs) was undertaken During operation he was given 550 ml gum acacia.

After operation his blood pressure was 65/35, and his pulse rate 128 So far he had received 550 ml saline per rectum—a total of 1,050 ml fluid At 3½ hr his ear haemoglobin was 63 5 per cent and his venous haemoglobin 61 per cent. Administration of fluid continued Blood pressure gradually rose and pulse rate fell, being 100/55 and 110 at 12 hr, and 125/60 and 96 at 24 hr For the first 22 hr he passed no urine

By about 33 hr after injury he had taken in 5,720 ml fluid and put out only 832 ml, haemoglobin was 50 per cent in both ear and vein

The only interpretation possible for this marked drop in haemoglobin from over 90 to 50 per cent is that the patient must have had a marked haemorrhage at the time of injury, losing almost half his total blood. Although there may have been shock in this case, and there probably was, yet his symptoms, low blood-pressure, collapse, etc., could all have been due to the tremendous and rapid reduction in blood volume.

Until near the end of the second world war there was no evidence from actual measurements made in man that "wound shock" is associated with reduction of blood volume, except that of Keith (1919a and b). Though the conclusion was accepted, the magnitude of the changes was regarded with some doubt because, as Gregersen (1946) points out, the blood volume methods were held to be unreliable, and because of the belief that increased capillary leakage in "shock" would vitiate the determination. (For further discussion and references see Gregersen, 1946.)

More recently the work of Gregersen and his associates and others has shown that the T1824 method can give sufficiently reliable measurements of plasma and blood volume, not only in normal subjects but also in those injured and "shocked" (for discussion and references see Part IV, Section A). Subsequent workers have used this method.

In 1943 Cournand *et al.* measured blood volume in a series of injured civilian patients, both shocked and not shocked; they report only the average findings in the different groups of patients, but Noble and Gregersen (1946b) deal more fully with the measurements. Their patients included 27 with skeletal trauma, 5 with abdominal injuries and 12 with haemorrhage from superficial and gastro-intestinal vessels; little information is given about the injuries and very few case histories. The criteria for the diagnosis of shock are not described. The authors conclude that "haemoconcentration is by no means a regular occurrence in shock from trauma". They found it in abdominal injuries with peritonitis, where they ascribe it to selective loss of plasma at the site of injury. But in skeletal trauma, as in simple haemorrhage, they put down the 30–40 per cent reduction in blood volume to loss of whole blood, and find that in both it is followed by haemodilution.

Evans, Hoover, James and Alm (1944) report blood volume measurements in injured civilian patients with and without shock. Only one very brief case history is given and the criteria for recognizing shock and assessing its degree are not stated. They conclude that "severe depletion of blood volume is the most important single factor in the causation of shock", and say that "signs of severe shock do not ordinarily appear unless the blood loss is greater than 15 per cent." The average loss in their cases of severe shock was about 38 per cent, no matter what the nature of the trauma. They found "no evidence of increased generalized capillary permeability" and say "it is evident that what is lost early in traumatic shock in the zone of injury is whole blood, not plasma".

Discussing the possibility of traumatic toxaemia, they emphasize that they "have seen the signs of moderate or severe shock appear in patients who have suffered any of four rather different types of body injury (acute blood loss, skeletal trauma, abdominal and chest injury) yet the degree of reduction of circulating blood volume in each of the groups was approximately the

same" But they point out that their observations contain "no evidence to exclude the possibility that toxic metabolites absorbed from the zone of injury in severe muscle trauma are not in part responsible for some of the shock picture"

Emerson and Ebert (1945) conclude from their study of blood volume (T1824 *method*) *in* 57 wounded soldiers that the average total blood loss estimated to have occurred in cases of severe shock before admission to hospital was as much as 63 per cent and was due to haemorrhage The majority of patients presented no evidence of an excessive loss of plasma, although this was found in a few cases with severe abdominal wounds and resulted in a mild degree of erythroconcentration

Our own chief finding is that in limb injuries and in the early stages of abdominal wounds before the onset of peritonitis reduction of blood volume by haemorrhage is the chief factor responsible for *illness* If traumatic or wound shock is taken to mean illness after injury, and if only limb and abdominal injuries are considered, then our observations are in accord with those of other workers

For further discussion of the blood changes following injury see Part IV, Section D

RELATION OF SIGNS AND SYMPTOMS TO BLOOD LOSS AND BLOOD VOLUME

We have already said that Keith (1919a) divides his cases of wound shock into three groups according to symptoms and signs, including blood pressure and pulse rate, and relates these to different degrees of blood volume reduction Robertson and Bock (1919a) from their study of blood volumes (vital red method) after haemorrhage suggest a rough method of estimating blood volume from the changes in blood pressure Their patients were 21 wounded soldiers suffering from the late effects of primary haemorrhage or from secondary haemorrhage, infection was present in the majority Blood volume was measured in 14, they tabulate data for 9 and quote representative examples in the text. Evans *et al* (1944) say that the trained observer can often estimate the plasma volume with surprising accuracy from the blood pressure level, the injury and the state of the patient Emerson and Ebert (1945), estimating blood volume in battle casualties, find that the character of the wound and the level of systolic blood pressure are the most helpful criteria, as do Chute's team (Cleghorn and Chute, 1945, and Chute, Cleghorn and Lathe, 1945) Noble and Gregersen (1946b) relate blood volume to the number of fractures

Our own findings reflect those of Emerson and Ebert (1945) and Chute the two signs that we have found to be of greatest value in limb injuries are, first and most important, wound size (index of blood loss) and, secondly, the level of systolic blood pressure (index of blood volume) In abdominal injuries we have to rely almost entirely on the second and less valuable of these two signs In both types of injury the information derived from the

blood pressure may be supplemented by that derived from the subsidiary signs of pulse rate, extremity temperature and face colour, and from other features such as thirst and restlessness. These criteria are now discussed further.

Wound Size

Wallace (1919) refers to "the well-known association between shock and small multiple, or single large muscle wounds". The suggestion was, however, that the "shock" was due, at least in part, to the absorption of some product from the damaged muscle (McNee, Sladden and McCartney, 1919).

Cowell (1919) divides wounds in their relation to the production of shock into three classes:

(i) Trivial wounds, such as slight scalp injuries or small lesions of subcutaneous tissues, which give rise neither to primary nor to secondary wound shock.

(ii) Moderately severe wounds, such as an uncomplicated fracture of the femur, a slight perforating wound of the abdomen or a lacerating wound of muscle without urgent haemorrhage, where primary wound shock is usually absent but secondary shock may develop later.

(iii) Serious wounds, which without prompt surgical attention would cause death, where symptoms result immediately and hypotension is found from the earliest moments.

Chute and his colleagues (Cleghorn and Chute, 1945) consider "the extent and situation of the wound . . . of prime significance in assessing the gravity of a case", but they do not define their criteria.

Noble and Gregersen (1946b) remark that in skeletal trauma "the total amount of blood lost . . . will in general depend upon the extent of muscle contusion, upon the number of fractures, and upon their relation to blood vessels". Their Figure 3 relates blood volume on admission to hospital to the number of fractures of the extremities sustained by the patient. It shows that single fractures are associated with blood volume reductions of up to about 20 per cent of the normal, two fractures with about 20–40 per cent and three or more fractures with over 40 per cent. There are no data that would allow us to classify the injuries in their cases according to our own categories.

Emerson and Ebert (1945) remark that the character of the wound was found "to be exceedingly helpful in estimating the degree of blood volume deficiency. Certain types of wounds, such as traumatic amputations, compound fractures of large bones, severance of major blood vessels, . . . are almost invariably accompanied by marked oligaemia". The greatest blood loss occurred in the patients with extremity wounds, only one of whom, a patient with multiple soft tissue shrapnel wounds, had lost less than 40 per cent of his estimated total blood. Their cases include only eight with extremity wounds alone, and again there are no data by which we might classify their cases within our scheme.

We have already said that in limb wounds we ourselves have found an estimate of the volume of tissue damaged to be a valuable index of blood loss.

The unit of volume is the patient's hand, and wounds are divided into four categories, namely

(1) small wounds, with a tissue damage of less than 1 hand,

(2) moderate wounds, with a tissue damage of 1 to less than 3 hands,

(3) large wounds, with a tissue damage of more than 3 but less than 5 hands, and

(4) very large wounds, with a tissue damage of 5 hands or more

With small wounds in general little blood is lost, commonly less than 10 per cent and rarely more than 20 per cent With large wounds, on the other hand, much blood is lost, of the order of 40 per cent, and with very large wounds as much as 50 per cent Moderate wounds give a less clear indication of blood loss, it may be much or little, though in the majority it is of the order of 20–40 per cent

The evidence from other workers, so far as it goes, supports our own, but is not enough to show whether this method of estimating wound size is likely to be useful to others besides ourselves We can only say that we, as our experience increased, came to rely on it more and more, and that when we dealt with abdominal injuries, where this index was not available, our clinical assessments of blood loss were more often at fault Wound size is of particular value as a sign because it is not, like blood pressure and the other circulatory phenomena, liable to be affected by other factors As we have pointed out, small wounds (unless a large vessel has been severed) may be taken as strong evidence against much blood loss even though the patient seems seriously ill On the other hand, even if the patient does not seem ill, large and particularly very large wounds, in the sense defined, almost certainly indicate gross blood loss and the urgent need for transfusion

It is clear, however, that much remains to be learned about the blood loss associated with different types of wounds Certain injuries are common but as yet we have little evidence of the blood losses usually associated with them

Blood Pressure

Keith (1919a) used systolic blood pressure as one of the signs for differentiating his three degrees of shock, but he did not indicate if it was the feature chiefly relied on In his "compensated" cases blood pressure remains above 100 mm Hg and blood volume is never reduced below 80 per cent normal In "partially compensated" cases blood pressure is as a rule below 90 mm Hg, usually 70–80, blood volume ranges between 65 and 75 per cent normal In "uncompensated" cases blood pressure is below 60 mm Hg and blood volume below 65 per cent normal Examination of his data, however, shows that they do not fully support his groupings in respect of blood pressure One of his 5 "compensated" cases (1 limb and 4 abdominal) had a blood pressure below 100 mm Hg, one of the 3 "partially compensated" (2 limb and 1 abdominal) had a blood pressure of 95 mm, and of the 14 "uncompensated" (12 limb and 2 abdominal) only 4 had blood pressures below 60 mm, the rest ranging up as far as 120 mm Hg

Robertson and Bock (1919b), working at a Base Hospital and also using the vital red method, measured blood volume in 14 wounded soldiers (data

charted for 9) who were suffering either from the late effects of primary haemorrhage or from secondary haemorrhage. They conclude that "blood pressure is of assistance in judging blood volume only when it is below a certain point, for there may be a considerable reduction of blood volume without any appreciable drop in the pressure".

Just how great a diminution can occur before the blood pressure falls cannot be stated, and there would seem to be some variation with the individual case In the present series we have had patients whose volume was reduced to 70 per cent of normal yet a normal blood pressure was still maintained. Such patients probably had some fall in pressure immediately after haemorrhage, since a blood loss of the amount indicated, unless very gradual, practically always causes a drop But the compensatory mechanism was able to restore the pressure to normal. The patients who had a reduction in volume below 70 per cent showed, with one exception, a blood pressure below normal, the decrease in blood pressure corresponding roughly with the amount of reduction in blood volume. The cases with a volume of 54 to 60 per cent of the normal showed systolic blood pressures of 70 to 80 mm. of mercury. One alone had a pressure of 90 mm. It is somewhat difficult to compare these figures, as the readings were not taken at the same intervals after haemorrhage, some being taken immediately and others after many hours or days. However, low blood pressure has been found to be associated so constantly with reduced blood volume that it seems fair to draw certain general inferences from these observations We have come to feel that in haemorrhage cases when a blood pressure is below 95 mm. the blood volume is probably under 70 per cent. With a blood pressure of 80 mm or less the volume is probably only 60 per cent or less. It is possible that a larger series of cases will show that these estimates need modification and that even more accurate inferences can be made from the blood pressure changes

Later writers agree in general that blood pressure is a valuable clinical index of blood volume deficit, but they differ as to how it may be used to assess the deficit.

Emerson and Ebert (1945) found that all cases with systolic blood pressure exceeding 100 mm. Hg had blood volumes of more than 75 per cent normal, while all with blood pressure under 85 mm. Hg had blood volumes of less than 75 per cent normal. Chute, Cleghorn and Lathe (1945) are less definite. They say that blood pressure was "the single most important sign of severe blood loss but if taken alone would often have been misleading"; they do not define the relation more closely. Evans *et al.* (1945), studying civilian casualties, found that if systolic blood pressure tends to remain below 90 mm. Hg "the chances are great that there has been a considerable blood loss."

Our own conclusion is that in untransfused cases with limb injuries, or with abdominal injuries without peritonitis, a blood pressure of over 140 mm. Hg indicates at least an 80 per cent normal blood volume, a pressure of 100–140 mm. indicates a blood volume of 70 per cent normal or over, and a pressure of less than 100 mm. indicates a blood volume about or below 70 per cent normal. In patients who have been transfused the blood pressure is a less reliable index, for the transfusion may shift it either above or below the level to be expected from blood volume. We have therefore examined further the data provided by those authors who, like us, have used the T1824 method. We omit those of Keith (1919) and Robertson and Bock (1919), because we cannot safely translate estimates obtained by the vital red method into

TABLE 32

Data from Chute, Cleghorn and Lathe (1945) *wounds of limbs or trunk not penetrating the thorax or abdomen*

Case	Nature of wounds	Hours since injury	Previous plasma transfusion (ml.)	Blood volume (per cent predicted normal)	Blood volume (per cent predicted normal × 1 05)	Blood pressure (mm. Hg)	Hand temperature
143	Traumatic *amputation of left foot*	½	—	100	105	170/84	Cool
1	Compound fracture of left femur	7	—	98	103	134/72	Warm
142	Perineum and buttock *compound* fracture of ilium	8	—	96	101	106/95	Cool
145	Compound fracture of left tibia dead leg soft tissue wounds	6½	2500	[illegible]	94	130/50	Warm
136	Compound *fracture of right tibia* multiple soft tissue wounds	3½	—	[illegible]	91	120/85	Cool
147	Laceration of flank compound fracture of ilium	20	—	87	91	156/84	Cold
130	Compound fracture *of left tibia* and fibula dead leg	27	1500	[illegible]	[illegible]	110/44	Cool
131	Compound fracture of right femur minor soft tissue wounds	[illegible]	—	85	89	110/75	Cool
17	Traumatic amputation *of left leg just* below knee	3	—	[illegible]	86	126/70	Warm
140	Large soft tissue and thigh and other minor wounds (Died of gas gangrene)	11	3500	82	86	90/50	Warm(T 103)
108	Large soft tissue wound *of right leg*	37	—	79	83	78/55	Cool
153	Traumatic amputation of left mid thigh compound fracture of right tibia	3½	1500	77	81	120/45	Cold
18	Compound fracture of *right femur and multiple* soft tissue wounds	43½	500	77	81	80/50	Warm
[illegible]	Fracture of transverse processes of 1st to 4th lumbar vertebrae haematoma	7	—	75	79	70/50	Cool
109	Compound fracture of *right femur*	28	500	75	79	60/50	Cool
107	Traumatic amputation of left foot minor peppering	14	1000	74	78	115/70	Warm
9	Compound fracture of *left femur radius and ulna* right tibia and fibula	6	—	74	78	78/55	Warm
106	Compound fractures of both femurs and right radius and ulna	19	1500	74	78	70/40	Hot (T 104)
155	Through and through wound of *left knee multiple* soft tissue wounds	?	—	73	77	110/70	Cold
5	Compound fracture of ilium and soft tissue wounds	6½	—	72	76	110/65	Warm
4	Compound fracture of left tibia and *humerus*	13	—	72	76	75/40	Warm
11	Compound fracture of right radius and ulna left tibia many soft tissue wounds	[illegible]	800	71	74	90/70	Cold
[illegible]	Compound fracture of right humerus *radius and ulna* dead arm	6½	750	70	73	74/60	Warm
7	Gross laceration of perineum and penis	6	—	67	70	76/?	Warm
13	Compound fracture of left humerus and *neck of scapula gutter* wound of buttock	3	—	67	70	60/45	Cold
111	Traumatic amputation of left forearm wounds of shoulder and scalp	32	500	67	70	86/50	Cold
12	Compound fracture of left tibia and fibula *multiple soft tissue wounds*	25	—	66	[illegible]	96/?	Cold
102	Compound fracture of right tibia, left radius and ulna soft tissue wounds	7	3700	66	69	140/85	Warm
3	Through and through flanks with paraplegia	13½	—	65	68	128/60	Warm
104	Gross lumbar wound compound fracture of right ilium	4½	—	65	[illegible]	58/40	Cool
114	Both legs grossly shattered below knees	4	—	65	68	40/?	Cold
[illegible]	Compound fracture of right fibula and left and right tibias many soft tissue wounds	6½	—	[illegible]	67	58/36	Cold
139	Soft tissue wound of right upper arm brachial artery torn dead arm	8	1600	60	63	82/55	Cold
110	Compound fracture of right tibia fibula and left calcis	5	1500	54	57	66/?	Cool
103	Compound fracture of humerus soft tissue wound of right leg	5½	—	52	55	50/?	Cold
118	Both legs grossly shattered below knee	[illegible]	—	46	48	Unobtainable	Cold

TABLE 33

Data from Clute, Cleghorn and Armstrong (1945): *wounds penetrating abdomen without gross lesions elsewhere*

Case	Nature of wounds	Hours since injury	Previous plasma transfusion (ml)	Blood volume (per cent predicted normal)	Blood volume (per cent predicted normal × 1 05)	Blood pressure (mm Hg)	Hand temperature
128	Two ½-cm slits in small bowel	2	500	97	102	160/80	Warm
125	Large through-and-through hole in transverse colon	3	—	97	102	160/70	Warm
157	Two small holes in jejunum and one in upper ileum	4½	—	95	100	140/88	Warm
148	Extraperitoneal hole in descending colon, compound fracture of ilium	17¾	—	94	99	125/85	Warm
113	Two transections of ileum	4½	1200	91	96	145/80	Cool
180	5-in tear in stomach	2½	200	89	93	110/75	Cool
135	Prolapse of small bowel, omentum torn off transverse colon	1	500	88	92	115/65	Cool
174	Right kidney torn, one hole in hepatic flexure of colon	5¼	1000 (+ 1000 blood)	88	92	96/90	Warm
124	Through-and-through wound of transverse colon, nick in right lobe of liver	4	—	87	91	155/80	Warm
10	Through-and-through wound of stomach, nick in left lobe of liver	9½	—	87	91	68/?	Cold
183	Four holes in hepatic flexure of colon, tear in edge of liver, penetrating chest wound	4	500	86	90	132/90	Cool
134	Eleven small holes in jejunum, one transection, one hole in sigmoid	1½	500	83	87	130/80	Cool
163	Two holes in jejunum, one in splenic flexure	4	200	80	84	86/?	Cold
123	Many holes in ileum, minor soft tissue wounds, penetrating chest wound	7	400	80	84	116/75	Cool
149	Transection of spleen, penetrating chest wound, soft tissue wounds	9½	—	79	83	135/80	Warm
182	Two 3in × 1 in × 1 in chunks of liver margin torn off	5	—	76	80	120/80	Warm
181	Gross tears in spleen and kidney, penetrating chest wound	2½	—	76	80	130/90	Cool
156	Holes in transverse and descending colon, through-and-through jejunum and stomach	19	—	75	79	142/90	Cold
119	Holes in jejunum, two rents in descending colon, compound fracture of sacrum	2½	—	74	78	100/68	Cold
170	Six holes in jejunum, through-and-through descending colon, compound fracture ilium, penetrating chest wound, other minor wounds	6	1100	73	77	60/?	Cool
112	Four large holes in terminal ileum, much blood	28	—	72	76	64/38	Cool
173	Many holes in lower ileum and one in caecum, peritonitis	9½	500	67	70	66/?	Cool
177	Many holes in gut	6	1500	65	68	70/?	Cold
116	Penetrating wound of right pleural sinus, liver damage and compound fracture of right ilium	3¾	—	58	61	35/?	Cool

TABLE 34

Data from Emerson and Ebert (1945): *limb wounds*

Case	Nature of wounds	Hours since injury	Previous plasma transfusion (ml)	Blood volume (per cent predicted normal)	Blood volume (per cent predicted normal × 0 95)	Blood pressure (mm Hg)	Pulse rate
43	Multiple shell fragment wounds of arm and thigh, survived	3	—	95	90	100/70	120
31	Shell fragment wounds with compound fractures of humerus, scapula and clavicle, survived	3	500	77	73	100/65	110
9	Gunshot wounds with compound fractures of humerus, mandible and zygoma, survived	2	—	63	60	70/40	130
5	Multiple shell fragment wounds of both thighs, survived	3	1150	58	55	100/60	136
19	Shell fragment wounds with compound fracture of femur, urethral transection, survived	5	500	56	53	80/55	128
28	Gunshot wound of thigh, lacerating femoral artery and vein, died 5 hr after admission	8	1400 (+ 500 blood)	54	51	50/0	120
18	Gunshot wound through axilla, severing brachial artery and vein, survived	3	750	54	51	70/40	124
48	Multiple mine wounds with compound fractures of right femur, right and left tibia and fibula, and right radius; died 5 hr after admission	6	750	49	46	60/0	100

TABLE 35

Data from Emerson and Ebert (1945) *abdominal wounds*

Case	Nature of Wounds	Hours since injury	Previous plasma transfusion (ml)	Blood volume (per cent predicted normal)	Blood volume (per cent predicted normal × 0 95)	Blood pressure (mm. Hg)	Pulse rate
41	Shell fragment wound penetrating abdomen laceration of spleen. Survived	3	—	98	[illegible]	170/90	80
27	*Shell fragment* wound penetrating abdomen liver laceration. Survived	3	—	97	92	130/80	180
[illegible]	Shell fragment wound penetrating abdomen multiple small bowel perforations Survived	2	—	96	91	100/60	96
6	Mine wounds penetrating abdomen *multiple* intestinal perforations Survived	3	750	94	89	130/70	104
30	Shell fragment wound abdominal with perforation of colon and evisceration Survived	4	250	[illegible]	86	95/60	140
33	Shell fragment wound penetrating abdomen no visceral perforations Survived	3	250	[illegible]	83	110/70	88
21	Shell fragment wound penetrating abdomen liver lacerated Survived	5	250	84	80	100/70	80
36	*Shell fragment wound penetrating* abdomen multiple perforations of bladder and small bowel compound fracture of coccyx Survived.	3	—	78	74	110/70	80
44	Shell fragment wounds penetrating abdomen multiple perforations of small bowel colon and bladder Died 8 hr after operation	2	—	78	74	90/80	104
35	Gunshot wound through abdomen perforating colon. Survived	2	500	76	72	120/80	96
34	*Shell fragment* wounds penetrating abdomen multiple perforations of colon and small bowel wounds of arm, face and scalp Died 14 hr after operation	2	500	76	72	140/90	96
42	Shell fragment wound penetrating left chest lacerations of diaphragm and liver haemothorax. Survived	5	—	75	71	140/70	108
1	Gunshot wound perforating rectum colon and small bowel Died 12 hr after operation	3	500	70	66	65/40	104
14	Gunshot wound through abdomen multiple perforations of colon and small bowel compound fracture of ilium Died 48 hr after operation	5	500	70	66	60/40	124
29	*Shell fragment wound* through chest and abdomen haemothorax lacerations of diaphragm spleen and kidney Survived	5	1000	68	65	95/50	144
46	Shell fragment wound penetrating chest lacerations of diaphragm and liver haemothorax. Survived	1	—	[illegible]	[illegible]	65/40	112
38	Gunshot wound through left flank with laceration of left kidney Survived	4	—	[illegible]	62	80/65	76
2	*Shell fragment* wounds of abdomen lacerations of colon and kidney Died 30 hr after operation	5	1150 (+ 1250 blood)	[illegible]	60	60/40	124
47	Shell fragment wounds *penetrating abdomen and* buttocks multiple perforations of small bowel compound fracture of right ilium Died 12 hr after operation	[illegible]	500	61	58	0/0	140
16	Shell fragment wounds with perforation of duodenum and inferior vena cava. Died ½ hr after operation	[illegible]	250	58	55	85/40	128
17	Mine wounds *penetrating* abdomen *multiple small perforations and mesenteric lacerations* Survived	3	500	52	49	85/50	160
11	Shell fragment wounds perforating duodenum colon liver and gall bladder Died ½ hr after operation	4	350	52	49	55/45	140
[illegible]	Shell fragment wound penetrating abdomen with multiple *perforations of small* bowel and colon. Died [illegible] hr after operation	5	1000	49	46	50/40	[illegible]

TABLE 36

Data from Evans et al. (1944): *skeletal trauma*

Case	Injuries	Blood volume (ml./kg.)	Blood volume per cent predicted normal (ml./kg. × 1.2)	Blood pressure	Pulse rate	Pulse quality	Extremities: Temperature	Extremities: Sweat
H.C.	Fractured femur	85	102	128/80	80	Good	Warm	Dry
O. R.	Compound fracture of femur and tibia	79	95	110/68	60	Good	Warm	Dry
D. T.	Fractured femur	78	94	120/80	80	Good	Warm	Dry
T. D.	Fractured femur	75	90	130/80	84	Fair	Warm	Dry
W. F.	Compound fracture of tibia and fibula	75	90	120/80	—	Good	Warm	Dry
I. D.	Fractured pelvis	74	89	120/70	90	Good	Warm	Dry
L. H.	Traumatic amputation of arm	73	88	130/90	82	Good	Warm	Dry
E. M.	Fracture of femur and base of skull	72	86	120/80	78	Good	Warm	Moderate
E. T.	Compound fracture of shoulder (gunshot)	70	84	120/80	76	Good	Warm	Dry
G. S.	Compound fracture of femur	70	84	90/60	70	Good	Warm	Dry
L. A.	Fractured femur, gun shot wound	70	84	90/70	76	Fair	Warm	Dry
P. H.	Fractured pelvis	69	83	130/80	—	Good	Warm	Dry
P. J.	Compound fracture of tibia and fibula	67	80	140/80	72	Good	Warm	Dry
C. W.	Fracture of femur	65	78	110/80	88	Good	Warm	Dry
A. O.	Fracture of pelvis	63	76	110/70	90	Good	Warm	Dry
S. H.	Compound fracture of femur	63	76	80/60	100	Fair	Cold	Moderate
E. W.	Fracture of pelvis	63	76	110/70	—	Good	Warm	Dry
M. N.	Compound fracture of tibia and fibula	62	74	124/82	90	Good	Warm	Dry
J. H.	Compound fracture of femur	61	73	60/40	60	Poor	Cold	Dry
H. T.	Compound fracture of femur	60	72	80/45	108	Poor	Cool	Dry
F. F.	Dislocated hip	59	71	130/90	90	Good	Warm	Dry
T. W.	Fracture of pelvis	58	70	70/50	136	Poor	Cold	Marked
L. M. S.	Traumatic amputation of foot & compound fracture of tibia and fibula	56	67	75/40	68	Fair	Cool	Marked
J. W.	Fracture of both ankles, compound fracture of humerus	55	66	80/50	108	Very poor	Cool	Moderate
G. R.	Fracture of tibia and fibula	51	61	80/40	80	Poor	Cold	Dry
L. F.	Fracture of femur and scapula	48	58	90/60	80	Good	Cold	Marked
T. L.	Compound fracture of tibia and fibula	48	58	92/50	76	Good	Cool	Dry
W. C.	Fracture of tibia and fibula	48	58	70/30	110	Poor	Cold	Moderate
P. R.	Fracture of pelvis and fibula	47	56	80/60	110	Fair	Cold	Marked
F. L.	Compound fracture of tibia and fibula and fracture of humerus	46	55	60/?	130	Poor	Cold	Dry
R. H.	Fracture of femur	43	52	70/45	100	Fair	Cool	Moderate
H. G.	Compound fracture of femur	42	50	58/40	140	Poor	Cold	Marked
S. C.	Fracture of femur and pelvis	40	48	88/60	100	Fair	Cold	Dry
E. K.	Compound fracture of tibia and fibula	32	38	82/70	116	Poor	Warm	Dry

TABLE 37

Data from Evans et al (1944) *acute blood loss*

Case	Blood volume (ml /Kg)	Blood volume per cent predicted normal (ml / kg × 1 2)	Blood pressure (mm Hg)	Pulse rate	Pulse quality	Extremities	
						Temperature	Sweat
J R.	79	95	90/60	76	Poor	Warm	Dry
A C	70	84	110/80	76	Good	Warm	Dry
R A	69	83	100/60	82	Fair	Warm	Dry
J H	68	82	120/80	80	Good	Warm	Dry
B E	67	80	110/80	120	Good	Warm	Dry
A E	63	76	92/70	96	Good	Warm	Dry
C C	60	72	92/66	80	Fair	Cold	Moderate
A R	56	67	60/40	80	Poor	Warm	Marked
W R	55	66	80/50	108	Poor	Cool	Dry

TABLE 38

Data from Evans et al (1944) *abdominal injuries*

Case	Injuries	Blood volume (ml /kg)	Blood volume per cent predicted normal (ml / kg × 1 2)	Blood pressure	Pulse rate	Pulse quality	Extremities	
							Temperature	Sweat
E P	Gunshot wound	82	98	130/80	98	Good	Warm	Dry
S P	Gunshot wound	78	94	140/100	90	Good	Warm	Dry
L F	Gunshot wound	75	90	124/84	123	Good	Warm	Dry
J M	Gunshot wound	70	84	90/70	120	Fair	Warm	Mild
L T	*Stab wound*	68	82	*128/80*	114	Good	Warm	Dry
D G	Stab wound of liver	68	82	120/80	100	Fair	Warm	Dry
S R	Gunshot wound	67	80	120/80	80	Good	Warm	Dry
H A	Gunshot wound	66	79	110/85	75	Good	Warm	Dry
E G	Gunshot wound	63	76	105/70	78	Good	Cold	Dry
A C.	Stab wound	58	70	80/50	84	Good	Warm	Moderate
W [illegible]	Gunshot wound	57	68	84/60 to 64/35	120	Fair	Warm	Dry
J T	Gunshot wound	55	66	140/100	[illegible]	Fair	Warm	Dry
H G	Gunshot wound	53	64	110/70	120	Poor	Cold	Dry
M T	Gunshot wound	49	59	60/40	95	Fair	Cool	Dry
A. M	Rupture of jejunum (traumatic)	45	54	75/50	120	Poor	Cold	Marked
W W	Rupture of jejunum (traumatic)	45	54	90/40	160	Poor	Cold	Marked

those obtained by the T1824 method. Chute's team (1945) and Emerson and Ebert (1945) dealt with battle casualties injured and seen in much the same conditions as those seen by us; Emerson and Ebert's cases were seen rather earlier. Most of Emerson and Ebert's cases and almost half of Chute's had previously been transfused. Evans *et al.* (1944) dealt with civilian casualties; the great majority of their patients were coloured, young or middle aged (no details given) and from lower economic levels. Their injuries were caused by knife and gunshot and by automobile and industrial accident. They were seen fairly soon after injury (no details given) and examined in the head-down position before treatment was begun. Their data may be used to supplement those from our civilian casualties in whom blood volume was not measured by the dye method.

From the tables given by these authors, we have abstracted cases of limb and abdominal injuries corresponding with our own, and reproduce the relevant data in Tables 32 to 38 with the cases arranged in the order of decreasing blood volume. To secure uniformity we have recalculated the results of all these authors in terms of our predicted normal values, which has in fact resulted in only small corrections. The derivation of our "predicted normal" values will be found in Part IV, Section A.

Emerson and Ebert and Chute's team tabulate estimated blood volume deficits in terms of predicted normal blood volume. We calculate that Emerson and Ebert's predicted normal values average 0 95 of ours and those of Chute 1·05 of ours. Their results have been recalculated to give measured blood volumes in terms of our predicted normal blood volumes. Evans *et al.* do not give total blood volumes, but give plasma volumes as ml. per kg and haematocrit values. Our predicted normal blood volumes correspond to an average of 78 ml. per kg To convert their values to percentages of our predicted normal, blood volumes derived from their plasma volume and haematocrit figures have been multiplied by 1 2 Their cases of acute blood loss may be grouped as limb injuries in our sense, they are instances of laceration of peripheral arteries and veins unaccompanied by muscle trauma From their cases as a whole we have excluded those with a haematocrit below 37 and plasma proteins below 6 0 g per 100 ml Since the patients were seen soon after injury, such low values may indicate a pre-existing anaemia or nutritional disturbance, and in such cases blood volume before injury was probably well below our predicted normal values.

The relation between blood volume and systolic blood pressure for the battle casualties of Emerson and Ebert, Chute's team and our own series is shown in Fig. 2 (untransfused cases) and Fig. 3 (transfused cases).

For the untransfused battle casualties, Fig. 2 shows that

(*a*) 68 of the 70 cases with a systolic blood pressure of 100 mm. Hg or more have a blood volume of at least 70 per cent of the predicted normal; in the remainder it is within 5 per cent of this, or "about 70 per cent normal".

(*b*) 10 of the 12 with a systolic blood pressure over 140 have a blood volume of at least 80 per cent normal.

It seems, therefore, that when blood pressure is 100 or more the chances are very great that blood volume is about 70 per cent of the predicted normal or more, and when it is above 140 the chances are about five to one that blood volume is at least 80 per cent normal.

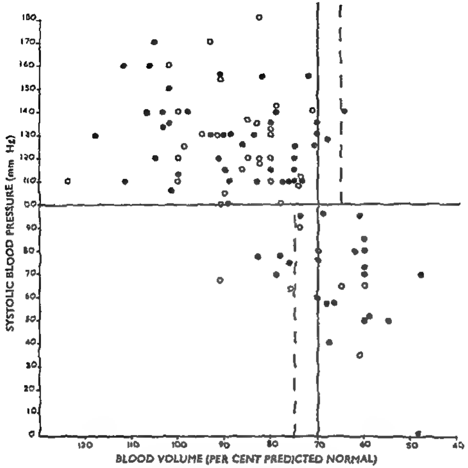


FIG 2 Systolic blood pressure related to blood volume untransfused battle casualties
● Patients with limb injuries
○ Patients with abdominal injuries

Eleven of the 28 patients with blood pressure below 100 mm also have a blood volume of 70 per cent normal or more, but in 5 of them it is below 75 per cent Hence we may say that 22 of the 28 have a blood volume of about 70 per cent normal or less Of the 6 exceptions it is to be noted that 4 were seen later than most (9½ and 28 hr for the 2 abdominal and 13 and 37 hr for 2 of the limb cases) and thus infection, rather than low blood volume, may have been responsible for the low blood pressure It can be concluded, therefore, that a blood pressure under 100 mm indicates that blood volume is about or below 70 per cent normal

In the great majority of battle casualties, therefore, a blood pressure of 100 mm Hg supplies a valuable dividing line

For patients who have already been transfused these rules for the interpretation of blood pressure in terms of blood volume are less reliable Fig 3 shows that, of those with blood pressures of 100 or above, there are more with blood volumes below about 70 per cent normal than among the untransfused, while similarly there are more with blood volumes above about 70 per cent normal in those with blood pressures below 100 This is to be expected from what has been said earlier about the effects of transfusion on the circulation The degree and direction of the side effect of transfusion on blood

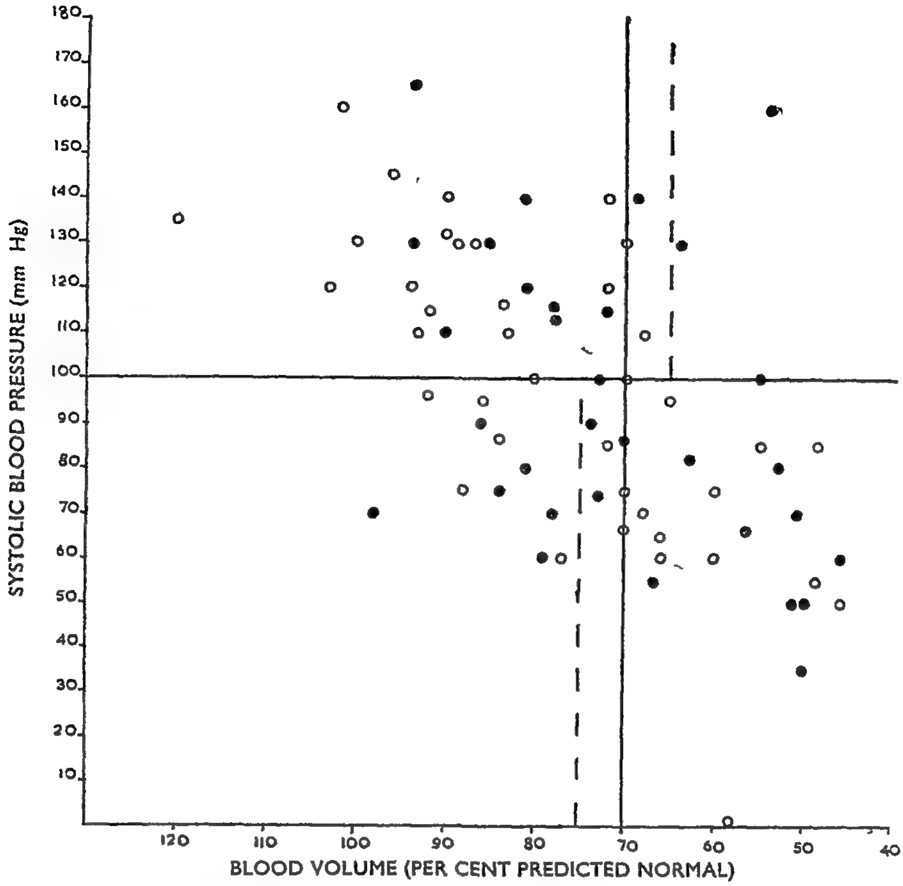


FIG 3. Systolic blood pressure related to blood volume transfused battle casualties
● Patients with limb injuries
○ Patients with abdominal injuries

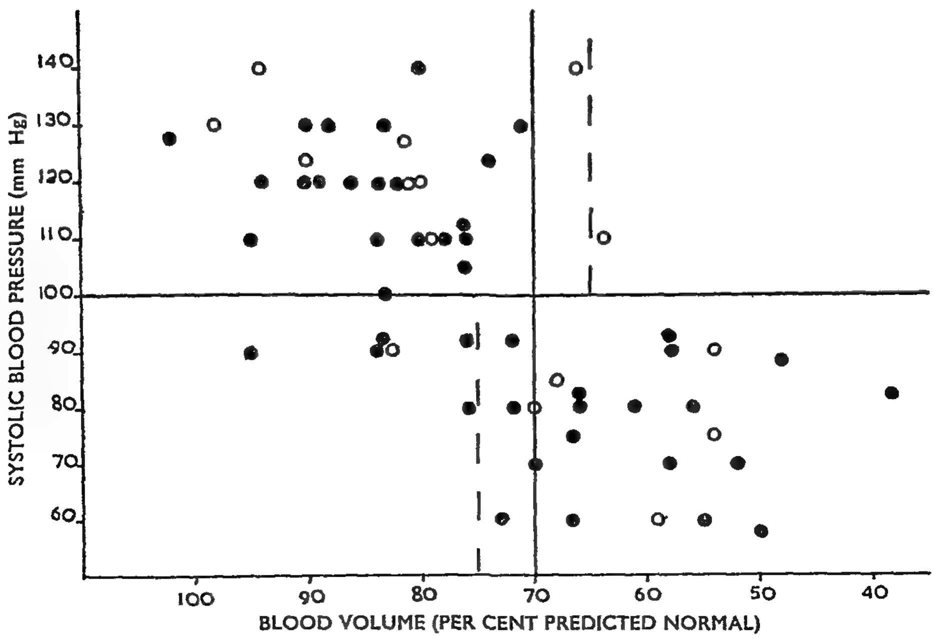


FIG 4. Systolic blood pressure related to blood volume· untransfused civilian casualties (data from Evans *et al*, 1944)
● Patients with skeletal trauma and acute blood loss
○ Patients with abdominal injuries

pressure depend on the pharmacological properties and the amount of the fluids transfused and on whether the patient is seen during the earlier constrictor or the later dilator phase of a transfusion reaction Hence transfusion may cause blood pressure to be either above or below the level expected from the blood volume alone

These data, derived from the work of three independent groups of workers, must be taken as fully representative of soldiers wounded in Europe during the last war They confirm the conclusions about the diagnostic value of blood pressure for assessing blood volume that we have already drawn from our series

Similarly in the civilian casualties of Evans *et al*, systolic blood pressure is a valuable index of blood volume and it is possible to apply the same rules Fig 4 shows that

(*a*) only 1 of the 30 patients with a systolic blood pressure of 100 mm Hg or more has a blood volume below about 70 per cent normal,

(*b*) of the 29 with a blood pressure below 100 mm Hg, only 6 have blood volumes above about 70 per cent normal To adopt the dividing line of 90 mm Hg for blood pressure, as do Evans *et al*, does not serve better to separate the cases, for, though all the cases with a blood pressure below 90 mm have blood volumes below about 75 per cent normal, so have a good proportion of those with a blood pressure of 90 mm or more So here too it is true that a blood pressure of 100 mm Hg supplies a valuable dividing line

Subsidiary Features

Combinations of Signs

We can find but little evidence dealing with these features as indices of blood volume Most writers relate them to the diagnosis of "shock" Keith (1919a), however, defined his three grades of "shock" by patterns of symptoms and signs and relates them to blood volume Thus the pattern of a blood pressure above 100 mm Hg, pulse rate of 90–110, and facial pallor he associates with a blood volume of not below 80 per cent normal According to our evidence, however, this pattern is more likely to be associated with a blood volume reduced to between 80 and 70 per cent normal The pattern of a blood pressure below 60 mm Hg, impalpable pulses and heart rate of 120–160 together with pallor, restlessness, great thirst and vomiting, Keith associates with a blood volume of under 65 per cent normal This corresponds with our picture of gross blood loss with a blood volume well under 70 per cent normal

Our own evidence shows that, while wound size and systolic blood pressure provide the main elements for the assessment of blood volume reduction, this assessment may be refined by information derived from the subsidiary signs of pulse rate, face colour and extremity temperature, and other features such as restlessness, thirst, dyspnoea and sweating (see pages 15, 18 and 100) As we have said, none of these features is of much value by itself, but combinations of them provide patterns of diagnostic value Further, we have defined some of the factors that may influence these features (cold, fear, pain, age, infection, transfusion, atropine, morphia) and thus disturb the relation they ordinarily bear to blood volume

Single Signs

(1) *Pulse rate.* Keith (1919a and b) does not himself discuss pulse rate alone, but examination of his data shows no close relationship between it and blood

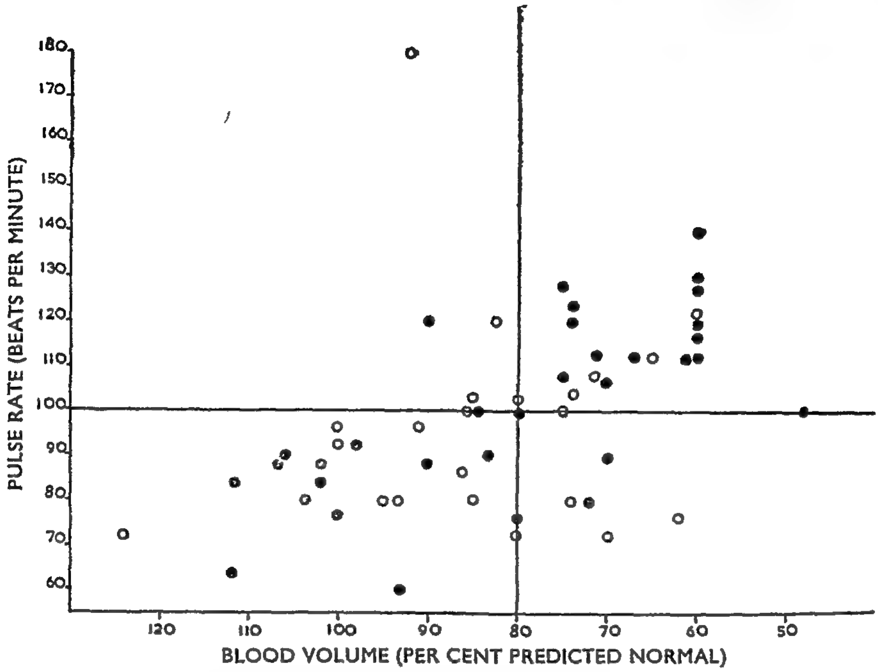


FIG 5 Pulse rate related to blood volume. untransfused battle casualties
● Patients with limb injuries
○ Patients with abdominal injuries

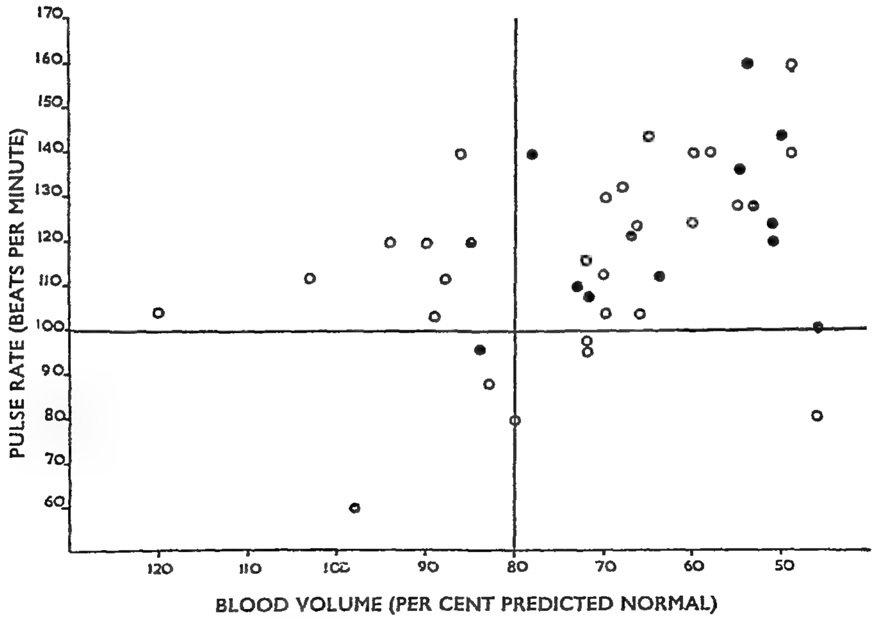


FIG 6 Pulse rate related to blood volume transfused battle casualties
● Patients with limb injuries
○ Patients with abdominal injuries

volume. Emerson and Ebert (1945) also find little correlation between the two: rates exceeding 130 were generally associated with a marked diminution of blood volume, but on the other hand several patients with severe oligaemia

did not exhibit tachycardia Evans *et al* (1944) point out that many patients with low blood pressure and seriously depleted blood volume have pulse rates more or less within the normal range However, our own opinion, gathered from their data and from our own, is that if transfused cases are excluded the pulse rate, though not of great value, is not so useless as is thought Figs 5 and 6 relate pulse rate to blood volume in the battle casualties of Emerson and Ebert and our series We exclude from our cases those given atropine or a similar drug shortly before examination For transfused patients, Fig 6 shows, as already pointed out, that tachycardia is the rule

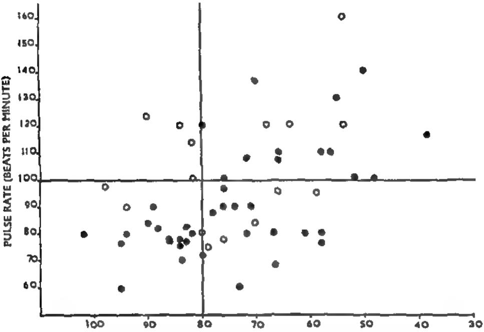


FIG 7 Pulse rate related to blood volume untransfused civilian casualties (data from Evans *et al*, 1944)
● Patients with skeletal trauma and acute blood loss
○ Patients with abdominal injuries

irrespective of blood volume But for untransfused cases, Fig 5 shows that only [illegible] of the 27 cases with a pulse rate of 100 or more have a blood volume well above 80 per cent normal, while only 5 of the 27 cases with pulse rate below 100 have blood volumes well below 80 per cent normal In the civilian cases of Evans *et al*, Fig 7 shows that again only 1 of the 21 cases with pulse rates of 100 or more has a blood volume much above 80 per cent normal, but 12 of the 35 cases with pulse rates below 100 have blood volumes well below 80 per cent normal That is to say, in both the battle and civilian casualties a pulse rate of 100 or more is a good indication that the blood volume is below about 80 per cent normal, but a pulse rate of less than 100 is not so clear in its implications, although usually associated with a blood volume of more than about 80 per cent normal, it does not exclude a considerably lower blood volume

(ii) *The remaining features* require little discussion Emerson and Ebert (1945) state that cold extremities and pallor were present almost universally,

and attribute them at least in part to the influence of pain and exposure to cold. We think it likely that another contributory factor is the prior transfusion, but this point cannot be determined from their data.

Both Chute's team (1945) and Evans *et al.* (1944) tabulate hand temperature and rate of filling of the forearm veins. We omit venous filling because in our experience cold hands are almost always associated with slowly filling veins. The data given by Chute for untransfused cases, and those of Evans *et al.*, agree with ours in showing that cold hands are the rule when blood volume is below 70 per cent normal. But since hand temperature is so readily influenced by other factors the sign is of little value by itself in assessing the level of blood volume.

Apart from noting that "paleness was frequently a characteristic of casualties that had bled a great deal," Cleghorn and Chute do not discuss facial colour, while Evans *et al.* dealt with Negro patients.

Cleghorn and Chute say that "sweating is not a feature . . . of long-standing oligaemia"; they recognize its occurrence in cases very recently wounded as part of the picture of syncope. The data given by Evans *et al.* show that profuse sweating is almost confined to cases with blood volumes below 70 per cent normal.

Chute's team note that thirst "was especially prominent in cases with severe blood loss" and that "nausea and vomiting were relatively infrequent, being . . . confined almost exclusively to the abdominal cases."

It might be thought that the development of a rapid and simple method* for measuring blood volume would obviate the necessity for using symptoms and signs as indications. But even when blood volume can be measured rapidly at the bedside, the extent of blood loss will still be doubtful until there is more knowledge about the normal blood volume in different age groups and states of health. Moreover it will very often be necessary to decide what treatment is required in circumstances in which blood volume cannot be measured.

Course Before Operation

The chief interest of this period lies in the treatment administered and the patient's response to it.

Keith (1919a) recognized that recovery from wound shock is associated with a rise in blood volume; that, while in slight cases the application of heat and the liberal administration of fluids by mouth are generally sufficient to restore the patient's condition sufficiently to permit operation, in many cases of severe wounds the blood volume must be raised by quick infusion, and that for this purpose whole blood is superior to saline solutions or to the gum acacia solution then used as a blood substitute. But, as Robertson (1919) points out, it was at that time "not possible to arrive at more than a tentative basis as regards the indications for and against the giving of blood." The widespread use of transfusion in war surgery was then new and there had been no time or opportunity to study carefully the cases who had been transfused.

*The method described by Gregersen (1944) seems likely to be serviceable, but we have no experience of its use.

He adds "we have no standard means of judging the severity of the patient's condition and each worker holds a somewhat different set of indications for and against transfusion from the other" This can be seen from the plans of treatment given by Keith and Robertson We have already described the categories into which each divides his cases (pp 184, 185)

Keith's plan is as follows

When the shock condition is *compensated* rest in a warm bed until the surgeon can operate is usually all the care necessary

The management of the *partially compensated cases* is more difficult The application of heat should first be given a trial If after one or two hours the pulse does not improve or the blood pressure rise, the question of increasing the fluid intake must be considered Fluid by mouth, except in small quantities as a mouth-wash, is contraindicated, for the ingestion of larger amounts soon leads to renewed vomiting Saline per rectum can be given as a routine measure on admission to the resuscitation ward but in order to obtain a more immediate response, when the trial of heat has failed, an infusion of 500 c c of gum solution is indicated The behaviour of the pulse and blood pressure is recorded at half hourly periods following the infusion If definite improvement persists for two or three hours, surgical treatment can be instituted However, if the improvement is only transient, a second infusion of gum can be administered, and frequently then a steady improvement follows, so that an operation can be performed, on the other hand, certain cases fail to respond to a second injection of gum, and if the haemoglobin percentage is low, whole blood transfusion should be given a trial.

It is chiefly in the *uncompensated cases* that infusions of gum solution and even transfusion of whole blood are of no avail

For his three categories, Robertson describes a rather different plan of treatment, which is as follows

Severe haemorrhage Immediate transfusion is indicated During the giving of the blood a recurrence of the bleeding should be watched for When a patient has lost so much blood that he has reached the very markedly restless stage, throws himself about the bed, and begins gasping for air, transfusion is too late Such patients may live for an hour or two, but usually die during transfusion or very soon afterwards

Moderate haemorrhage and shock These are difficult cases in which to decide the best course to pursue, since some recover sufficiently to be operated on if left alone, while others apparently in the same condition do very badly In the *severe cases* that are brought in pulseless and cold, it has been found advisable usually to observe for some time the effect of the ordinary restorative measures Under the influence of warmth and rest they may begin to pick up very promptly, and within several hours will have improved sufficiently for operation The majority of these patients, however, who do respond do not improve rapidly It usually takes one or more hours If at the end of one or two hours there is no improvement or only very slight improvement, transfusion is given Experience has shown that, as a rule, such cases do not pick up to any marked degree without assistance A dusky appearance has been noted as indicating that such a patient will probably not improve unless transfused The *moderately severe cases* of haemorrhage and shock—i e those who still have a pulse though feeble, and a low pressure on admission, usually improve under warmth and rest and sleep Many of them make rapid progress, and in a comparatively short time are fit for operation Others improve to a certain degree, then remain stationary for some time, or may begin to relapse very soon A small number show no improvement whatsoever The general method of procedure in this class of case is to allow the patient to recover by himself if possible, but not to let his chance of recovery slip away by too long waiting As long as the patient is making steady and rapid progress it is usually wise to withold transfusion If at the end of two or three hours progress slows up

definitely, and he is still some distance from an operative condition, transfusion should be given On the other hand, if after an hour or two of watching the patient shows none or only very slight improvement, or at any time begins to lose ground, he should be transfused at once.

Shock The chief need in this class of case is an increase of blood volume. The circulation contains ample haemoglobin carrying material, but the blood is concentrated and the pressure is too low to carry the blood through the tissues in sufficient amount. When transfusion is given to these patients it is with the idea that this is the best means available for raising the blood pressure. Therefore it would seem advisable, on account of the fact that results from transfusion in shock are much less satisfactory than after blood loss, to give a preliminary trial to other suitable fluids more easily procurable than blood, keeping the blood in reserve if these fluids fail to bring about sufficient restoration. Certain cases of shock are very definitely benefited by blood, but it is not at all improbable that a suitable fluid substitute might accomplish the same result. The procedure of observation followed in cases of moderate haemorrhage and shock applies equally well to this class of case.

Robertson also stated the views then reached about the amount to give, the rate of transfusion and its effect on the patient, and the time of operation.

[*Amounts of blood to be given.*] The extent of the blood loss is the best general indication as to the size of the transfusion needed. Cases of marked haemorrhage are found to do much better after transfusions of 900–1,000 c c. than after smaller amounts To cases of moderate anaemia 600–700 c.c. may be given. It is always better, when in doubt as to the need of the individual case, to give a large transfusion Cases of shock are usually given 500–600 c c.

[*Rate of transfusion*] Ten to fifteen minutes is the time usually taken for the introduction of the average amounts of citrated blood or preserved blood cells. With large amounts it is advisable to slow up the blood flow towards the end of the transfusion . . . If at any time the patient shows signs of distress—difficulty in breathing, a sense of internal pressure or pain in his chest, the transfusion should be slowed up or stopped till these symptoms, which are usually quite transient, pass off.

[*Effects of transfusion.*] The blood pressure has been found to be the most reliable index of the condition and especially of the progress of a case . . . Pulse rate is of much value in certain cases of haemorrhage, but in the majority of cases complicated by shock it gives little information as to the actual condition present. On the other hand a rise or fall in blood pressure indicates with considerable accuracy the direction the case is taking . . .The rise in blood pressure following transfusion may be immediate and marked, but more often it takes some little time for the full effect of transfusion to become apparent. The response is most prompt in cases of haemorrhage. With shock or shock and haemorrhage the rapidity with which the improvement takes place seems to depend largely on the length of time the condition has existed Cases that have been in shock for many hours often show surprisingly little immediate effect from transfusion but improve progressively during the next hour.

[*Time of operation*] It is generally agreed that with a systolic blood pressure of 85 to 90 mm Hg operation can, as a rule, be performed with safety. Some place 90 as the lowest figure that is consistent with safety However, this varies with the kind of anaesthetic employed . . .

It is the custom in some Casualty Clearing Stations to transfuse immediately before or during operation In cases of pure haemorrhage operation immediately after transfusion is probably a safe and wise procedure, since this class of case picks up so rapidly after the introduction of new blood. This is most certainly the course to pursue if the patient is still bleeding at the time of transfusion . . . It is also desirable in cases suffering from internal haemorrhage not to transfuse until the bleeding cavity is opened However, in conditions complicated by shock (which conditions

constitute the majority of cases presenting themselves for transfusion), it would seem much better to delay operation until the benefit from newly introduced blood has become well marked In many cases this will occur within half an hour, in others it may take an hour or even longer, depending on the condition present before transfusion

It has been observed that individuals who have remained in a state of low blood pressure for many hours are very liable to develop extensive gas gangrene subsequently Thus it would seem advisable to limit the pre-operative period to 3 to 4 hours at most whenever possible

At this same period Robertson and Bock (1919b), in discussing the treatment of haemorrhage, made the following important suggestion

We have shown that the blood pressure may be normal with a blood volume reduction of 25–30 per cent, and that unless the volume is reduced below this point there may be no drop in pressure The maintenance of a normal pressure with a diminished volume depends entirely on a vasomotor mechanism which is responding well to the increasing demands made by these abnormal conditions The circulatory balance may be on the verge of profound disturbance, but as long as the patient is quiet and at rest the compensation is held However, if an increased strain is put on a circulation in this condition, such as an anaesthetic, operation, infection, or recurrence of blood loss, the vasomotor mechanism may fail and a drop in blood pressure result We have not had opportunity to study in detail many instances of this kind, but have observed several cases in which there was a good blood pressure with a reduced volume, and whose reaction to increased strain seemed to be the result of the mechanism suggested above

They cite briefly one case which we quote, piecing together the data given in their text, chart and legend to the chart

Case 3, aged 18 years, wounded the day before, had a compound comminuted fracture of the right femur extending into the knee joint and a history of haemorrhage

Operation, lasting ¾ hr, began 24 hr after haemorrhage It consisted of amputation through the fracture, very little blood was lost except in the amputated limb

At the start of operation blood pressure was 105/70, pulse rate 100 By the end of operation, blood pressure had fallen to 70/40 and pulse rate risen to 120 Blood volume was then measured and found to be 70 per cent normal He was given 580 ml 6 per cent gum acacia solution, when his blood pressure rose in 10 min to 110/50 and his pulse rate slowed to 80 Blood pressure was maintained, and the wound healed without sepsis

They remark that although "the blood volume was not taken before operation there is no reason to suppose that it changed much during this brief period as there was very little blood lost except in the amputated limb", and add, "It would seem in this instance that had the blood volume been a little greater the drop in pressure might have been avoided If these inferences are further substantiated it is obviously important to restore the blood volume beyond simply raising the blood pressure"

These quotations show the state of knowledge about the pre-operation treatment at the end of the first world war So far as we can find, nothing material was added to it up to the time of the second war Methods of preserving and storing blood were improved and new transfusion fluids—plasma and serum—were introduced, while the increasing use of transfusion in medical cases led to emphasis on the danger of pulmonary oedema arising from too fast and too much transfusion But matters of such great practical importance in dealing with injured patients as the indications for transfusion,

the type and the amount of fluid to be transfused and the time at which to operate are not discussed in the monographs of Moon (1940) or Scudder (1940) or in Blalock's book (1940).

It is evident from the quotations that the choice of treatment depended on the diagnosis of the patient's state; for severe hæmorrhage blood transfusion was recommended, for hæmorrhage and shock, or shock alone, rest, warmth, fluids and observation and transfusion later if necessary. The confusion and uncertainty that existed at the beginning of the second war about diagnosis thus made it difficult to decide how injured patients should be treated. Others besides ourselves felt the need for better indications. For example, Kekwick *et al.* (1941) say that though "the obvious treatment for shocked patients is to restore the blood volume, information is required as to the best fluid for this purpose, when to transfuse, in what amount and at what rate." At that time, too, the importance of Robertson and Bock's suggestion was not clearly recognized. Thus McMichael (1941) says only that transfusion of blood, plasma or serum should be given until the blood pressure is normal. Kekwick *et al.* too, though they recognize that "reduction in blood volume demands a reasonably quantitative replacement of protein fluid," say that in general "the amount to be transfused should be governed by the blood pressure" and consider that their results "confirm the accepted clinical belief that transfusion should be continued until the blood pressure has been satisfactorily restored." They warn that "over-enthusiasm for quantitative replacement has its dangers, for an overfilled circulation is almost as great a menace as one which is dangerously emptied." Their impression is:

> that 2 pints can be administered quickly without risk to a case of secondary shock with a blood pressure below 100 mm Hg. If this produces the anticipated rise in blood-pressure more can be administered with safety, though if the clinical condition has equally improved the rate of administration can be judiciously slowed [one bottle in 3 to 4 hours]. But if there is no improvement in blood pressure with 2 pints quickly administered, and continued bleeding is neither obvious nor likely, a short time should be allowed for warmth and fluid by mouth to bring about that later improvement in blood pressure which a number of cases appear capable of effecting. This is better practice than continuing with a large rapid transfusion which carries with it a danger of pulmonary oedema if the circulation is overfilled The rate of administration after the first 2 pints requires sound clinical judgment But whenever there is clear evidence of gross loss of blood an approximately quantitative replacement should be aimed at.

It has already been pointed out that, as the second world war progressed, there was an increasing realization of the great part played by haemorrhage in producing "shock", and transfusion came to be given earlier, more rapidly and in much greater amounts than previously; its use was extended to cases not yet "in shock", but in whom "shock" was latent or impending. But it was not until relatively late in the war that measurements by the T1824 method gave more accurate estimates of haemorrhage and showed that it was much greater and that blood volume was much more reduced than was commonly thought. The correlation of these measurements with various clinical features allowed the statement of more precise rules for assessing

reduction of blood volume which offered a better indication for treatment than had existed hitherto

Of those who have measured blood volume by the T1824 method, Cournand *et al* (1943), Evans *et al* (1945) and Noble and Gregersen (1946) do not deal with treatment, the only workers to consider this are Chute's team (1945) and Emerson and Ebert (1945)

They recognise, as we do, that restoration of blood pressure does not mean that blood volume also is restored to normal, and that further amounts of transfusion must be given after the blood pressure has been raised to 100 mm Hg or more Chute, Cleghorn and Lathe record observations on 17 cases showing blood pressure at or above 105 mm Hg when blood volume was calculated to average 16 per cent below normal, and draw the conclusion that "individuals who have lost much blood and come in with low blood pressure and poor peripheral circulation should receive approximately 1,000 c c of blood or plasma after the blood pressure rises to normal levels" The general plan followed by Emerson and Ebert in preparing casualties for operation was "(1) patients with normal blood pressure but with severe wounds suggesting a significant degree of blood loss were given 1,000 ml blood, and (2) those with low blood pressure attributable to blood loss were given 2,000 ml blood, or, if an adequate response was not attained, 1,000 ml more than the amount required to restore systolic blood pressure to approximately 100 mm Hg From blood volume determinations both before and after such transfusion they found that in most instances oligæmia had been accurately corrected"

Our own estimate of the amount of transfusion required is based on

(1) the estimate of blood loss and blood volume derived from wound size and the level of systolic blood pressure, supplemented by other subsidiary features,

(2) an estimate of the amounts by which the transfused fluids may be expected to increase blood volume, which, in the case of a bottle of plasma, blood or serum, would be by about 5, 8 or 9 per cent respectively of the average normal blood volume,

(3) the response of the patient's systolic blood pressure to transfusion The systolic blood pressure is first raised to about 100 mm Hg, by which time the blood volume is presumed to be about 70 per cent of the predicted normal, this will be true only if the transfused fluid has provoked no strong vasoconstrictor reaction, for such a reaction can raise blood pressure to 100 mm Hg or above while blood volume is still below 70 per cent normal,

(4) the level to which it is desirable to restore blood volume Those patients do best at operation and subsequently whose blood volume is maintained well above the critical level of 70 per cent normal, 80 per cent will allow them to pass through operation successfully, but 90 per cent allows a better margin of safety and should generally be aimed at

We doubt if transfusion of the amounts advised by Chute *et al* or Emerson and Ebert would in practice suffice to restore *normal* blood volume Chute's team used the same fluids as we did, and their suggested transfusion of 1,000 ml of plasma or blood would be expected to raise blood volume by about

10–16 per cent respectively of the average normal. Almost all the blood used by Emerson and Ebert was diluted with an equal volume of glucose-sodium-citrate-saline preservative (Alsever's solution) but, from the context, it seems clear that when these authors speak of giving "1,000 ml. blood" they mean blood without added diluent. The average haematocrit reading of the stored blood, correction being made for the added preservative diluent, was approximately 50. It is unlikely that 1,000 ml. of blood of this haematocrit would increase blood volume by more than about 20 per cent of the average normal. It appears from their observations that even such large volumes as 1–2 litres of saline solution rapidly leave the circulating blood and do not increase the blood volume. Thus the amounts indicated by these two groups of authors would probably, according to our findings, result in raising blood volume to between 80 and 90 per cent rather than to normal or above.

It has been pointed out that while these data provide a satisfactory indication of the amounts to be given in the majority of cases, others, particularly those with very large wounds, may require larger amounts.

Emerson and Ebert warn against excessive transfusion and say that no case should receive more blood or plasma than is required to restore the blood volume to normal: they consider that the finest clinical judgment is often needed to ascertain at what point transfusion should be stopped. In our experience, however, this difficulty does not often arise before operation. In the first place, few patients with injury either to limbs or abdomen fail to exhibit a satisfactory rise of blood pressure in response to transfusion. Secondly, if a patient does fail to respond, no advantage is to be gained by delaying operation in order to pursue transfusion, for it is better to proceed with surgery so that the bleeding or infection that may be causing the therapeutic failure can be dealt with rapidly. We are in agreement with Emerson and Ebert and with Chute *et al.* that these are the chief causes of failure to respond to transfusion. Another, less frequent, cause is too great a delay in beginning transfusion.

According to Emerson and Ebert one of the earliest indications that the replacement therapy has been more than adequate, or has been prosecuted too vigorously, is the development of neck vein distension; on the appearance of this sign, transfusion must promptly be halted if pulmonary oedema is to be averted. They quote two cases of limb injury in which transfusion was followed by neck vein distension, cyanosis, frank pulmonary oedema and death. Chute's team, on the other hand, saw no instance of overloading of the circulation in limb injuries before operation, nor do they refer to its occurrence in abdominal injuries. We ourselves did not see neck vein distension or pulmonary oedema in either limb or abdominal cases before operation.

The reasons for the development of pulmonary oedema are not fully understood, but it seems that other factors than overtransfusion may be involved. In neither of the two cases of pulmonary oedema quoted above from Emerson and Ebert was blood volume raised above normal limits, while others of their cases were transfused greater amounts more rapidly and did not develop pulmonary oedema. For example we quote two of their cases, piecing together the data given in the text, tables and diagrams.

Case 48 was admitted 6 hr after injury with multiple mine wounds of both legs, including compound fractures of one femur and of both bones of both legs

Previously transfused with 750 ml plasma, his blood volume on admission was 2,390 ml (red blood cell volume only 580 ml) or 46 per cent of the predicted normal (our standard), his blood pressure was 60/0 and his pulse rate 100

Over about 4 hr he was transfused with 2,300 ml blood and 1,450 ml diluent, his blood pressure was then 102/20, his pulse rate about 130, blood volume was 5,010 ml or 96 per cent normal He was then transfused with approximately 500 ml blood (diluent?) but blood pressure fell Livid cyanosis and neck vein distension developed and then frank pulmonary oedema, death occurring 5 hr after admission

Case 1 was admitted 3 hr after injury with wounds of the right buttock penetrating the abdomen, the rectum, colon and small bowel were perforated, and there was massive faecal contamination of the peritoneum

He had been transfused with 500 ml plasma and his blood volume was 3,810 ml (red blood cell volume 1,580 ml) or 66 per cent normal (our standard)

Over the next 2½ hr he was transfused with 250 ml plasma, 2,500 ml blood and 2,500 ml diluent, blood volume was then 6,270 ml or 109 per cent normal, blood pressure was 150/80, pulse rate about 100 The response to transfusion was excellent

The patient went to operation (lasting nearly 3 hr) 4 hr after admission His condition after operation was satisfactory, but blood pressure again fell and he died 12 hr later, apparently from overwhelming peritoneal contamination

The authors attribute the failure of response to transfusion in *Case* 48 to prolonged tissue anoxia and suggest that the venous congestion and pulmonary oedema were due to myocardial failure We suggest that another possible factor is gross pulmonary fat embolism which, as our observations have shown, is liable to occur in cases with such extensive limb injuries Necropsy findings are not recorded

Keith (1919b) remarks that in 8 of his 29 cases the original condition of shock tended to persist and would seem to have been the cause of death He believed that, when gum acacia infusion or blood transfusion failed to improve the circulation, the failure was due to the inability of the vascular system to retain the added fluid His data, however, would now be interpreted otherwise For example, he cites the following case to show that a transfusion of 880 ml blood raised blood volume by only 150 ml and adds that shortly afterwards the patient died during operation We piece together the data given in the text and tables (there are discrepancies which, however, are immaterial)

Case A H, aged 19 years, had gunshot wounds in both lower legs and a shattered lower leg He was seen 7¼ hr after wounding, when his blood pressure was 75/40 and his pulse rate 128, his blood volume was 2,540 ml or 55 per cent normal (Keith's value) and his haematocrit 33 per cent

At 10½ hr blood pressure was 80/60 and pulse rate 136 He was transfused 880 ml whole blood

At 12 hr there had been no more external bleeding, his blood pressure was 130/15, his pulse rate 120, and the clinical improvement was striking, blood volume was 2,690 ml, or 59 per cent normal, and haematocrit 32 per cent

At 12½ hr the right lower leg was amputated At 12¾ hr, during operation, the patient died

Necropsy showed oedema of lungs, all organs were very moist, though not actually oedematous

It now seems likely that this case is an example of gross blood loss responding well to transfusion but later collapsing and dying because transfusion was inadequate.

Our data have also provided strong evidence that it is bad practice to delay transfusion, as was done in the first world war and in the early stages of the second, and have emphasized two other points:

(1) In any case of hypotension with limb and soft tissue injury it is unwise to delay transfusion unless there is prompt recovery in the head-down position.

(2) In cases with a marked degree of circulatory failure (blood pressure under 70 mm. Hg, usually a very rapid heart rate, great pallor, cold extremities and often great restlessness and dyspnoea) there must be no delay in beginning transfusion if life is to be saved. It was known in the first world war that cases of gross haemorrhage urgently require transfusion, but it is clear from the views and examples quoted that gross blood loss was very often not recognized as such but was diagnosed as "shock".

Course During Operation

Though references to the occurrence of shock during operation on wounded patients in the 1914-18 war are frequent, they give little detailed evidence about circulatory changes. The tables of Drummond and Taylor (1919) and of Keith (1919b) show the blood pressure and pulse rate before and after operation: in a number of cases the blood pressure fell and the pulse rate rose during operation. Marshall (1917), who worked at a Casualty Clearing Station, also remarks on the possible fall of blood pressure during operation and, in abdominal cases, relates this to various factors.

> If the operation involves much manipulation of the gut and pulling on the peritoneum, the pressure will fall. This fall, however, is slow and the process may be continued for hours without reducing the blood pressure to a dangerous level
>
> Exposure of the gut outside the abdominal cavity produces a much more serious effect on the patient. If more than two or three feet of gut are so exposed, after a few minutes the blood pressure commences to fall and it continues falling until the gut is returned to the abdomen This effect is seen when the stomach and omentum are exposed, and even with the great omentum alone. The covering of exposed viscera with pads soaked with hot saline does not prevent this effect on the patient's condition. Nevertheless it seems probable that the cause is heat loss from the exposed blood vessels Exposure of gut produces much less effect on a man not under an anaesthetic He has seen men arrive from the line with several feet of intestine prolapsed through a wound yet their blood pressure was within normal limits. In one case, more than two-thirds of the small gut had been outside the abdominal cavity for at least 4 hours, yet this man's blood pressure was 142 mm. of mercury and his pulse rate only 108, the patient recovered.
>
> Apart from copious haemorrhage, there is one other procedure which causes a rapid fall of blood pressure during abdominal operations. This is turning the patient on his side. The effect is produced only if the patient has been under the anaesthetic for a considerable time before being turned. At the end of an abdominal operation the patient may be in good condition, he is then turned on the right or left side, in order that the surgeon may excise a wound in the back. In a few minutes there is a great fall of blood pressure and the radial pulse disappears. It may be hours before the patient [illegible] ground.

Phemister and Livingstone (1934) give, under the heading of neurogenic shock, a brief account of the blood pressure and pulse rate changes during surgical operations in civilian patients These changes are seen particularly in operations on the upper abdomen for lesions of the stomach, duodenum and biliary system, but are much less often seen in operations on the lower abdomen and have not been observed with the same certainty in operations on other parts of the body

> Fall in blood pressure even to low shock levels with slight bradycardia may take place during opening and exploration of the abdomen or during the performance of the intra-abdominal part of the operation, and in the complete absence of blood loss
>
> The blood pressure usually declines rapidly during the early part of the operation, beginning sometimes during the abdominal incision The pulse rate is either unchanged or slightly slower than normal The blood pressure usually rises either late in the intra-abdominal procedure or during closure of the abdomen and by the time the operation is over it is often up to the pre-operative level
>
> If other circulatory depressive factors are superimposed, as haemorrhage and poor anaesthesia, and the operation is prolonged, secondary shock of grave concern may set in, and call for additional treatment by blood transfusion or physiological saline injections

In our cases, circulatory changes were very common during operation on patients with injuries to the limbs as well as those with abdominal wounds They were more varied and more complex than is suggested by the above quotations Thus increase or decrease in the level of blood pressure was often accompanied by either dilatation or constriction of the cutaneous vessels, and by either increase or decrease of the pulse rate So far as we could determine, the factors mainly responsible for these changes were the surgical manipulations of the injured parts, the nature and method of administration of the anaesthetic agents, the blood loss and the transfusions at operation For example, surgical manipulation may provoke either a rise or a fall of blood pressure in limb injuries but apparently only a fall in abdominal injuries, the pulse and cutaneous changes are various Again, the different anaesthetic agents give rise to different vascular changes, ether, cyclopropane and chloroform may all provoke a fall of blood pressure associated with cutaneous vasodilatation, the pulse rate is increased by ether, a little slowed by cyclopropane and markedly slowed by chloroform, "Pentothal" appears not to influence the cutaneous vessels though it may on occasion lower blood pressure and increase pulse rate On the other hand, the administration of the volatile anaesthetic agents through an anaesthetic machine and mask may cause a persistent rise of blood pressure, probably because of some degree of respiratory obstruction, the withdrawal of the mask at the end of operation is then accompanied by a rapid fall of blood pressure In most cases several factors operate on the circulation at once and it is often not possible to determine what part each plays in provoking the observed vascular changes Further analysis under more simplified conditions is required to define the precise effects of a particular factor

Marshall (1917) considers the suitability of different anaesthetics for limb and abdominal injuries

For the lightly wounded, gas and oxygen seem best; ether however was the most generally useful anaesthetic. For limb cases suffering from shock, if chloroform is used, the patient is likely to die on the table. With ether the patient's condition actually improves during operation, but he will collapse an hour or two afterwards. Incomparably good results are obtained with gas and oxygen and no other anaesthetic should be used for this type of case. Anaesthesia may be so light that the patient will move when nerves are resected. There is practically no evidence of shock from the operation, even when there is an amputation through the upper part of the thigh. In few cases did the blood pressure fall 15 mm or the pulse rate rise more than 10 beats per minute. The patient is fully conscious five minutes after operation. There is no collapse during the next few hours, and the subsequent progress is notably good.

For abdominal cases warm ether and oxygen is best. The quiet induction, easy breathing and diminished heat loss leave the patient in remarkably good condition at the end of a long operation. The blood pressure shows a tendency to rise. With chloroform blood pressure falls steadily and if operation be prolonged the patient may die before the abdomen is closed or shortly afterwards.

Crampton (1922) expresses himself in similar terms and in addition emphasizes the need for skilful administration of the anaesthetic, especially of gas and oxygen. Neither Marshall nor Crampton gives sufficient evidence to support his views.

In the recent war, anaesthetists preferred "Pentothal" for lightly wounded patients with limb injuries, but ether for the more seriously wounded and for abdominal wounds. Beecher (1945) holds that ether is the anæsthetic of choice for the seriously wounded, while "Pentothal" should be avoided when shock is present or anticipated. He does not give evidence in support of these statements nor have we found adequate evidence elsewhere.

Our own observations provide no data on which to express preference for any anaesthetic, but stress the need for skilful administration of whatever anaesthetic agent is used. They lead, however, to the suggestion that "Pentothal" anaesthesia renders the circulation less liable to falls of blood pressure with surgical manipulation than does ether. They suggest also that the preference for nitrous oxide in the first world war was probably due to the fact that then transfusion was often either inadequate or non-existent, and patients reached operation with blood volumes near or below the critical level. In such patients it is to be expected that gas-oxygen would tend to maintain or even raise blood pressure while ether would make it fall.

We have already drawn attention to the suggestion by Robertson and Bock (1919b) of the importance of raising blood volume above the level at which blood pressure is restored to normal, so that the patient may better withstand the increased strain put on his circulation by an anaesthetic, operation and further blood loss. So far as we can find, this suggestion has not been dealt with since: of those who have measured blood volume by the T1824 method, none except ourselves has described the events at operation. But we have provided much evidence to show the prime importance of the level of the blood volume during operation in determining the circulatory state. The various factors acting on the circulation, the anaesthetic, the surgical manipulation and the renewed bleeding, are all more liable to provoke a collapse of the circulation if the patient's blood volume is near the critical level of 70 per cent normal than if it has been raised well above this level.

Further, it has been shown that even patients with very large tissue damage can pass safely through a long and difficult operation provided blood volume is well above the critical level, 80 per cent normal or more Hence it is important to ensure that before operation the patient's blood volume is raised well above the level needed to restore blood pressure, and also, since renewed bleeding during operation can easily reduce a blood volume near the critical level to below this level, thus precipitating a fall of blood pressure, it is important to continue transfusion during operation itself

Haemorrhage at operation may be considerable, though in our experience not so great as that found by Emerson and Ebert (1945) In one case involving debridement of multiple wounds of thigh and foot they estimate blood loss to have been 1,270 ml, and in five laparotomies they estimate the average blood loss to have been 2,200 ml These estimates were derived from measurement of blood volume before and after operation, but they give no details of the time intervals between the operation and the measurements From their Fig 5 it seems that in one of their cases the intervals were about 1 hr before and 7 hr after operation, so that the blood loss may not have been confined to the operation alone They give no details of the events at operation Our own estimates were made by collecting blood shed at operation, and in both limb and abdominal injuries we found blood loss to be usually well under 500 ml In the exceptional case a litre of blood or more might be lost, but in such cases the surgeon had always had difficulty in controlling the the obviously considerable bleeding

Another factor that renders the circulation unstable and enhances the effect of the depressor factors at operation is the presence of infection But our observations here are incomplete and further work is required

Course After Operation

EARLY POST-OPERATION PERIOD

Little is to be found in past writings about the events during this period in injured cases Robertson (1919) says that at this stage "cases in collapse present a somewhat different problem from the newly admitted case in need of resuscitation The majority of these patients had been in moderately good condition before operation Their subsequent poor condition is due to the operative procedure with in many instances increased loss of blood Cases in whom the collapse is acute and severe need transfusion immediately Others in less critical condition, particularly those who have been given ether or chloroform, are watched for an hour or more to determine whether the depression might not be due to the anaesthetic used If at the end of this time there is no improvement, they are transfused"

Chute and his team report observations on both limb (Cleghorn, Chute and Lathe, 1945a) and abdominal cases (Cleghorn, Chute and Lathe, 1945b) after operation Like us, they stress the need for careful watching and frequent blood pressure estimations for 12–24 hr after operation. They also find that the chief illness of this period is a circulatory failure shown by low blood

pressure, fast pulse rate and poor peripheral circulation. It was usually associated with a blood volume about or below the critical level, but it appeared in a few of their cases when blood volume was well above critical level or even normal. These cases, as Emerson and Ebert (1945) and we ourselves have also found, were mainly those with infected wounds. Chute's team draw attention to a few other cases in which a low blood pressure was associated with a good blood flow through the extremities and a blood volume well above the critical level or even above the predicted normal, but can offer no explanation. Most of their cases and all ours with this circulatory pattern recovered.

They also provide evidence that blood may be lost from the circulation without external haemorrhage. Their studies show a disappearance of up to half a litre of red cells between pre- and post-operation blood volume measurements; they feel that such a change could not be due entirely to blood loss at operation, although they give no estimates of the latter. The point is further discussed in Part IV.

In the majority of patients with hypotension the blood pressure is restored within an hour or two of operation. But in a few, particularly those with very large limb injuries or infected abdominal wounds, hypotension may persist beyond this period in spite of apparently adequate transfusion. In such cases it is particularly important that blood volume should be raised well above the critical level (70 per cent normal), and at the same time blood pressure is an unreliable index of blood volume. There may therefore be much doubt whether or not to continue transfusion, and the doubt can only be resolved by actual measurement of blood volume.

Chute's team (Cleghorn, Chute and Lathe, 1945b) point out that three of their abdominal cases with hypotension associated with blood volume above normal were transfused excessively. They say that "it seemed better to overfill a slack circulatory bed as the risk of not doing so seemed greater than the danger of provoking congestive failure", and consider that the results supported the hypothesis. Of this, however, we are doubtful. Two of the cases did develop signs of congestive failure, one dying from pulmonary oedema, the other recovering. The third case also died, apparently from renal failure and pneumonia.

It is clear from the observations of Chute's team, Emerson and Ebert and ourselves that if adequate transfusion fails to restore the circulation no other effective remedy is available.

LATE POST-OPERATION PERIOD

About this period, too, little is to be found in past writings. The frequent occurrence of anaemia and hypoproteinaemia has been noted, for example by Cleghorn, Chute and Lathe (1945a and b) and Stewart and Warner (1945). These authors note also the renal insufficiency that may develop in both limb and abdominal injury cases.

Our own observations are incomplete and serve mainly to draw attention to a field of work which, in contrast to that of the earlier stages of illness, is relatively unexplored.

It has been seen that during this period circulatory failure is no longer the chief illness and that patients who continue to be ill suffer from such factors as metabolic, erythrocytic and renal disturbances, infection and fat embolism

It is clear that renal disturbance can arise from various causes, but in our series the chief factor seemed to be blood loss and insufficient transfusion in those with limb injuries and a metabolic disturbance brought about by gastric suction in those with abdominal injuries Chute's team consider none of these to be of major importance, but offer no other explanation

We discuss in Part IV, Section G, the metabolic disturbances brought about mainly by gastric suction and inadequate fluid and salt replacement Here we will only say that others, for example Stewart and Warner (1945), note that dehydration, with consequent oliguria, azotaemia and hypochloraemia were frequent in those with abdominal injuries and that they consider disturbances of fluid balance a challenging problem in surgical after-care

Deaths and Necropsy Findings

Our series of patients was small and selected, and we know of no others comparable on which to base a discussion of the deaths and post mortem findings It may be noted, however, that other workers attribute a considerable proportion of the deaths after abdominal injury to "shock" and a relatively small proportion to infection For example, Blackburn and Rob (1945) list shock and haemorrhage as the causes of death in 48, or about 62 per cent, of their fatal cases, while Porritt (1945) lists shock as the cause in 358, or about 39 per cent, of 912 fatal cases Porritt uses "shock" to describe the cause of death in those severe cases that never picked up after operation, Blackburn and Rob do not define their use of the word From Table VIII of Blackburn and Rob it appears that about 28 per cent of their cases died from some infection, and from Table XIV of Porritt that about 16 per cent died from this cause The cause of death is unknown in a further 24 per cent of Porritt's cases It has been seen that in our 35 fatal abdominal cases death is attributed to haemorrhage alone in 1 instance only and to haemorrhage with infection in 4 others The chief cause of death is infection, which was mainly responsible for 18 deaths and partly responsible for a further 9 We have suggested that in many cases infection was aided by salt and water shortage

Our observations after death are of interest mainly in supporting or correcting the interpretation put on the cases during life, either by confirming that no important lesion had been overlooked or by revealing some unexpected complication

The chief unexpected finding was the presence of pulmonary fat emboli in all cases dying from limb injuries and in a high proportion of those with abdominal injuries Our observations during life and after death show that the part played by pulmonary fat embolism in causing death after injury is hardly better understood than it was in 1889 by Cohnheim, who remarked that when a man dies within 24 hr of receiving a fracture it is doubtful whether

or not death is to be attributed to the fat emboli almost invariably found in the lung vessels. Some, for example Killian (1931), hold that while pulmonary fat embolism may exceptionally be the main factor responsible for death soon after injury, a more frequent cause is the combination of fat embolism and "shock". If "blood loss by haemorrhage" is substituted for "shock", then the problem is put in a form that opens a way to further observation. It may be that early death after injury is often brought about by the combination of a degree of pulmonary fat embolism and a degree of haemorrhage neither of which would alone be sufficient to cause death.

Hitherto the possibility of death being partly due to pulmonary fat embolism has rarely been considered until after death. If further evidence is to be obtained, injured patients must from the beginning be studied with the possibility of fat embolism in mind.

Circulatory Patterns

In Parts I and II numerous case histories have been quoted to show the clinical pictures seen in patients suffering from limb and abdominal injuries. It will have been noted, first, that circulatory disturbances form an important part of these pictures and, second, that these disturbances afford evidence valuable for diagnosis and treatment. It is important, therefore, to recognize them, their circumstances and their significance. This may not seem easy because they are so various, so grade into each other and are due to such a variety of factors. But, if finer detail be excluded, they fall into a few patterns that are easy to recognize by circulatory signs that recur from time to time during the course of illness and have special significance.

The four signs used to characterize these patterns are (i) the level of systolic blood pressure, (ii) the pulse rate, (iii) the temperature of the extremities and (iv) the face colour. Blood pressure is defined as normal when the systolic value lies between 100 and 140 mm. Hg, as raised when it is over 140 and as low when it is below 100 mm. Hg. Pulse rate is defined as normal when it lies between 70 and 99 per minute, as fast when 100 or more, and slow when under 70.

The *normal circulatory pattern* is defined as a normal blood pressure, a normal pulse rate, warm extremities and a good face colour. In injured patients this is associated with little blood loss and a blood volume nearly normal. In patients with larger blood loss, this pattern is ultimately restored by adequate treatment.

The main disturbances of the normal pattern are six. In two the blood pressure is normal, in one it is raised and in the remainder it is low. For ease of reference names are suggested by which these patterns might be called.

(1) The pattern of *cold tachycardia* is a normal blood pressure, a fast pulse rate, cold extremities and usually a pale face. It is met with chiefly in the first few hours after injury and is then commonly associated with a moderate blood loss and a blood volume reduced to between 70 and 80 per cent normal. It is also the pattern associated with the constrictor phase of a transfusion reaction.

(2) The pattern of *warm tachycardia* is a normal blood pressure, a fast and bounding pulse, warm extremities and usually a well-coloured, but sometimes a pale face It is associated with a blood volume of 70 per cent normal or over and is met with (i) in the dilator phase of a transfusion reaction and (ii) in injured patients in whom haemoglobin has fallen to very low levels

(3) The *hypertensive pattern* is a raised blood pressure and usually a normal or slow pulse rate The extremities may be warm or cold and the face well-coloured or pale It is associated usually with a small blood loss and a blood volume of 80 per cent normal or more Usually transient, it is often met with soon after injury but may also occur before and during operation if suitable stimuli are applied

(4) The *vasovagal pattern* is a low blood pressure, a slow pulse rate, cold extremities and a pale face To these may be added sighing respirations, sweating, nausea and vomiting It is commonly met with soon after injury, is transient, and is due to sensory and emotional stimuli rather than to blood loss Less commonly it occurs both before and during operation when suitable stimuli are applied Occasionally it is associated with much blood loss and may be seen as a terminal pattern in patients dying from haemorrhage

(5) The pattern of *cold hypotension* is low blood pressure, a fast pulse rate, cold extremities and a pale face It is found in two types of cases (i) It is commonly seen in patients whose blood volumes are reduced by haemorrhage below 70 per cent normal, and then tends to persist until abolished by transfusion In patients with great blood loss and a blood volume reduced below 60 per cent normal an extreme form develops, namely, a very low blood pressure (under 70 mm Hg), impalpable pulses and a very rapid heart rate, cold extremities with constricted veins and pale face and lips To these may be added great restlessness, dyspnoea, and sweating This form indicates the need for immediate, large, and rapid transfusion to save life (ii) It is met with in patients suffering from a heavy infection, such as advanced peritonitis, and in them may be associated with a normal blood volume and is not abolished by transfusion Here the pulse rate tends to be faster and the extremities warmer than when haemorrhage is the provoking factor

(6) The pattern of *warm hypotension* is low blood pressure, a fast pulse rate, and warm extremities The face may be flushed, well-coloured or pale This state is usually, but not always, transient Blood volume is generally reduced, although not below 70 per cent normal The factors provoking it are not properly understood It is usually met with in warm surroundings, often after operation, when it is thought to be due to a combination of factors such as the anaesthetic agent (ether and cyclopropane), body warming and the previous transfusion It is not uncommon during operation, when ether and cyclopropane are probably the factors concerned, and is sometimes brought about by undue body warming before operation

The use of these patterns makes diagnosis more precise and guides treatment better than the use of the prevailing idea of "shock" To bring them all under the one term "shock" is only possible if this is taken to mean no more than the "general effects of injury", in which case the statement that a

patient is "shocked" can convey no precise diagnosis of his state and indicate no particular treatment. The alternative is to restrict the term "shock" to only one of these patterns, say, that of cold hypotension; this would not only depart from common usage but would also emphasize unduly one particular pattern of the many that are possible.

To use these patterns in dealing with injured patients also serves to direct further work. Though the patterns are known, the factors provoking them are not fully understood and the mechanisms by which these factors provoke their effects are largely unknown. For example it is not known how apparently identical sensory and emotional stimuli can produce on the one hand the vasovagal pattern and on the other the hypertensive, nor how the differing factors of haemorrhage and infection may both give rise to the one pattern of cold hypotension. Knowledge of these mechanisms should advance treatment: for example, it should help us to treat cold hypotension due to infection, for which at present no remedy is known despite the fact that the same pattern when caused by haemorrhage can be cured by transfusion.

Conclusion

As has been shown, the contradictory statements made about shock and the lack of adequate description of shocked and injured patients had led to confusion. To discover the facts behind the contradiction and confusion required renewed study.

Parts I and II of this report contain a full account, illustrated by numerous examples, of 230 patients suffering from injuries to the limbs and of 80 patients suffering from injuries to the abdomen. The injuries were sustained in air raids, in battle, at work and on the roads. Emphasis has been laid throughout on the symptoms and signs found not only when the patients were first seen but also at later stages, before, during and after operation. Those who died were examined after death.

By these observations, made over a period of five years, we have become intimately acquainted with some of the features of the illness brought about by two types of injury in the circumstances of the last war. Much has been learned that could not be learned from past writings. It is now known which of the features are common and which are rare, how they are related to each other, to the age of the patient and to the type of injury, and how they change in the course of the case. Critical examination of these features and of their relation to each other, to the injuries, and to estimates of blood volume and blood loss have led to conclusions about the factors responsible for the illness and have also shown how the injuries, symptoms and signs can be used at the bedside to assess how ill the patient is, what will happen to him and what treatment he requires.

The observations of others, published during and since the last war, have led to many of the same conclusions. But so far as we are aware there is no comparable study of a series of cases of limb and abdominal injuries followed in detail from the time of admission to hospital until recovery seemed assured

or until death With few exceptions the recorded observations of others have been almost confined to the initial state of the patient and its response to treatment It is thought, however, that the widening of this study to include the later course of the illness has led to an account of the general effects of injury, particularly those on the circulation, which forms a connected and consistent whole

PART IV

CLINICAL PATHOLOGY

By E. B. Reeve

A. Measurement of Blood Volume and Estimation of Haemorrhage

In the preceding parts of this Report the clinical state and course of injured patients have been related to blood volume and haemorrhage estimates, and these estimates have been used as a guide to transfusion, in some cases massive transfusion. In this section the methods used to estimate blood volume and blood loss are described and the value and meaning of such estimates in normal persons and the injured are assessed, while in the next section the size of transfusion required by those with very large injuries is discussed.

METHOD OF ESTIMATING BLOOD VOLUME

Blood volumes were estimated with the dye T1824. Attempts to estimate blood and total red cell volumes with the Ashby marked red cell method failed through lack of facilities for preserving strong agglutinating sera.

Dye

The T1824 used was a single sample obtained from Imperial Chemical Industries, Ltd. When tested by the "capillary" filter paper test it showed only a very faint trace of a red component. Sterile 0 5 g. per 100 ml. solutions in distilled water were prepared and diluted before injection to form about 0·2 g. per 100 ml. solutions in isotonic sodium chloride. Volumes of these solutions of 12–20 ml., measured with an accuracy of $\pm$ 0·2 ml., were injected.

Sampling

Blood samples were withdrawn with no or minimal stasis into oiled syringes, and the blood was gently transferred to centrifuge tubes containing heparin. A sample of undyed blood was first obtained, and through the same needle the dye was injected into the vein. Subsequently, further samples were obtained, usually at 15 min. intervals after the injection of dye, from veins remote from that into which the dye had been injected. Samples were withdrawn from veins of the forearms or upper arms, or from the external jugular or femoral veins. Veins were chosen through which there was an adequate blood flow and from which there was little difficulty in sampling.

So far as possible plasma volumes were estimated while the circulation (during the 45 min. or more of the estimation) was in a relatively steady state Thus plasma volume estimations were not made during periods of rapid transfusion; if transfusion could not safely be stopped, it was run very slowly during the estimation Periods of much circulatory change, such as the onset of rigors or considerable haemorrhage, were avoided, as were

periods of very marked vasoconstriction, when it was difficult to obtain a sample from a peripheral vein Great care was taken with blood sampling

Unfortunately it is not possible to make blood volume estimations at the time of greatest interest in the very severely injured patient, that is, when he has marked and progressive circulatory collapse, since if rapid transfusion is withheld his life may well be lost But in patients with systolic blood pressures persisting in the region of 70 mm Hg apparently reliable plasma volume estimates may readily be obtained

Estimation of Dye Content of Plasma

Two methods were used in estimating the plasma dye content.

Direct Method

This was the method of Gibson and Evelyn (1938) with some modifications The optical densities of the dyed plasma samples were measured with a photo-electric photometer and the red colour filter used by Gibson and Evelyn With this red filter there is a slightly curvilinear relationship between dye content and optical density With each plasma volume estimation a standard was also estimated, prepared by adding 0 1 ml of a suitable dilution of the same dye solution as had been injected to 1 5 ml of the undyed plasma Much care was taken in the accurate preparation of this standard, and its dye content was close to the dye contents of the dyed plasmas Dye contents of standard and samples were read from calibration curves

The photo-electric photometer used measures a difference of 0 01 mg dye per 100 ml plasma, i e about 1 per cent of the concentration of dye ordinarily found with the amounts of dye injected Errors in the estimate of T1824 content of a series of plasma samples may be caused by variations in plasma cloudiness and plasma haemoglobin Cloudiness and variations in cloudiness in the samples are readily detected by observing the scattering of a parallel beam of light passed through them If plasmas so examined were seen to be more than a little cloudy, or if there was a slight variation in the cloudiness observed in a series of samples, the second method of dye estimation was used

To minimize possible effects of small variations in cloudiness, rather large amounts of dye (25–30 mg) were injected, and since fat tends to separate from the plasma on standing, particularly at low room temperatures, the dye contents of samples were estimated usually within 2–4 hr of drawing them Fortunately, plasma samples obtained from patients with moderate sized or large wounds within 48 hr of wounding were usually free from cloudiness

The amounts of plasma haemoglobin found, the errors they caused and the correction of these errors are discussed under the second method

T1824 in plasma may be decolorized or altered in colour by oxidizing and reducing agents (Phillips, 1943, and personal observations), and it is possible that this may occur either *in vivo* or after the withdrawal of blood from the body The latter is probably rare, and repeated estimations made on the same samples at different periods after withdrawal showed no evidence of loss of colour

To check the constancy of composition of the samples of blood drawn for a blood volume estimation, haemoglobin, haematocrit, plasma protein and plasma haemoglobin were determined on all samples. Haemoglobin was determined by the first method described by Reeve (1944), haematocrit by spinning in tubes of the dimensions of Wintrobe's tubes at 3000 r.p.m. at approximately 1500 × gravity for 30 min., plasma protein by the copper sulphate specific gravity method of Phillips *et al.* (1943) but using the amended formula $P = 360\ (G_p - 1{\cdot}0070)$, and plasma haemoglobin by the benzidine method. One hundred per cent haemoglobin was taken as 16 g. haemoglobin per 100 ml. blood*.

Extraction Method

This was the method of Crooke and Morris (1942), in which T1824 is extracted into an ethanolic hydrochloric acid phosphotungstic acid reagent.

Certain criticisms of this method can be advanced. (*a*) Variations in completeness of the extraction of the samples of a single plasma volume estimation will cause error. (*b*) Haemoglobin pigments are changed into acid haematin and extracted with the dye by the reagent, and acid haematin has an appreciable absorption of light in the red end of the spectrum. (*c*) The reagent is light-sensitive and on exposure to daylight forms a coloured compound with an appreciable absorption in the red end of the spectrum. Moreover Morris (1944) reports that certain specimens of phosphotungstic acid contain a substance which causes the photo-chemical oxidation of T1824 to a colourless compound. (*d*) 1 ml. of dyed plasma is diluted with 7 ml. of the reagent, so that the dye is diluted eight-fold and light absorption in the red is rather weak.

The advantage of the method is that clear extracts can be obtained from cloudy plasma solutions, and in practice we found it fairly satisfactory.

The procedure used differed in a few minor respects from that of Crooke and Morris. To check the completeness of extraction and guard against photochemical effects, an additional standard and blank were included in each plasma volume estimation. The extra standard consisted of 7 ml. of the reagent, 1 ml. of water and 0·1 ml. of the dilution of the injected dye used in preparing the dyed plasma standard. The blank consisted of 7 ml. of the extraction reagent added to 1 ml. of water. Duplicate extractions were made on some, and often all, of the plasma samples and the dyed plasma standards. The preparation of the reagent, the extractions and the photometric estimations of dye content were carried out with very little exposure to light, either natural or artificial, and such light as was used was dim; no photochemical effects were detected in the course of these estimations. Plasma samples were usually extracted within 3 hr. of the injection of dye into the patient. The extracts were thoroughly spun, allowed to stand and then respun, and readings of dye content were made at periods between 4 and 24 hr. after the injection of dye. All extracts were examined for

*For standardization, the haemoglobin contents of ten samples of blood drawn from ten healthy subjects were determined by the copper sulphate specific gravity method of Phillips *et al.* (1943), the specific gravities of both plasma and whole blood being determined

cloudiness, but careful handling and sufficient spinning always resulted in clear solutions being obtained Dye concentration was estimated by the photo-electric photometer with the red filters used in the first method In this spectral region there is a straight line relationship between concentration of dye in extracting reagent and light absorption

Crooke and Morris (1942) quote one experiment in which the dye content of a plasma dye standard extracted with the reagent was found to be identical, within the errors of measurement, with that of a water standard of similar volume and dye content treated with the reagent They therefore assume that the reagent completely extracts dye from plasma Our observations do not support this In 75 plasma volume estimations by Crooke and Morris's method recovery of dye was 80–90 per cent complete in 5, 90–95 per cent complete in 30, and 95–100 per cent complete in 40 The cause of this varying extraction of dye from differing plasmas was not determined To minimize possible effects of differences in extraction of dye from the samples of a single plasma volume, the control plasma dye standard was made to have a dye content close to that of the dyed plasma samples obtained from the patient, most samples were estimated in duplicate, and all standards and samples were put through the extracting process simultaneously and as nearly as possible under the same conditions Agreement between duplicates was good Ninety per cent of them differed by less than 2 per cent of the sample total dye content and it was rare for them to differ by as much as 5 per cent

In a number of blood volume estimations the dye contents of the plasma samples were estimated by both methods and good agreement was found Thus, in 27 estimations uncomplicated by cloudiness or significant amounts of plasma haemoglobin, plasma volumes determined by the two methods agreed within $\pm$ 3 per cent in 21 instances and within $\pm$ 5 per cent in 24 instances, in 3 instances they differed by $+$ 6 per cent, $-$ 7 per cent and $+$ 10 per cent respectively, the first method being taken as the standard When possible the first method was used rather than the extraction method because of its greater ease and precision, but a quarter of all estimations were made by the extraction method

Haemolysis

The liberation of small amounts of haemoglobin into the plasma by haemolysis interferes considerably with the extraction method but little with the direct method The amounts of haemoglobin in all samples for plasma volume estimates were determined by a simple quantitative modification of the benzidine method of Ingham (1932) In 85 per cent of all samples the haemoglobin content was no more than 10 mg per 100 ml, an amount that can safely be neglected In the remaining 15 per cent more than half had between 10 and 20 mg haemoglobin per 100 ml and the rest had between 30 and 300 mg per 100 ml The greater contents of haemoglobin resulted usually from breakdown of red cells in the circulation after transfusion of faultily stored blood, and in two instances probably from a mismatched transfusion, but occasionally they were due to errors in technique In the

first case the haemoglobin contents of all the samples of a plasma volume estimation were usually identical, and automatic correction was given by the control plasma samples used in both methods of blood volume estimation.

As we have already said, small amounts of haemoglobin are quantitatively extracted as acid haematin by Crooke and Morris's extracting reagent, and for concentrations of haemoglobin of the order found there is a straight line relationship between the absorption in the red (the same filters being used as in both methods of blood volume estimation) and the quantity of acid haematin. An extract of plasma containing 100 mg. haemoglobin per 100 ml. plasma has an absorption in the red equivalent to that of 0·25 mg. T1824 per 100 ml. plasma, and when the haemoglobin content of the plasma is known this relationship may be used to correct for the presence of differing quantities of plasma haemoglobin in the samples of a blood volume estimation. In practice it was rarely necessary to apply such correction. No corrections were required for the haemoglobin contents of the dyed plasma samples estimated by the first method.

It is thought that the errors introduced into our estimates of the plasma dye contents by the presence of haemoglobin pigment were at most small.

Correction for Dye Loss

Correction was made by extrapolation for dye lost between the time of dye injection and plasma sampling. The plasma dye contents of a series of samples taken at intervals from 15 min. after dye injection were determined and plotted against the times of withdrawal, and the best straight line was drawn through them to estimate dye concentration at zero time. Samples were not taken till 15 min. after dye injection so as to allow adequate time for "mixing"; Noble and Gregersen (1946a) report that the average "mixing" time of injected dye in the plasma of injured persons suffering from shock is 15 min. It has been claimed that dye is lost from the circulation in the first few minutes after injection (Cruickshank and Whitfield, 1945) and that morphine causes an abnormal disappearance of dye (Bowler, Crook and Morris, 1944), but neither claim could be confirmed (Reeve and Armin, 1946).

In 30 blood volume estimations on normal or mildly injured subjects the loss in the first hour (i.e. the period between 15 and 75 min. after the injection of dye) varied between 5 and 9 per cent of the total dye, with plasma concentrations varying between 0·8 and 1 8 mg T1824 per 100 ml.

In injured, particularly severely injured, patients the circulation did not remain in a steady state for as long as an hour, so samples were withdrawn over periods of 20–45 min. In a number of instances two samples only were withdrawn after dye injection, but this procedure was found to be justified, since in patients with widely differing abdominal and limb wounds estimates based on extrapolation from the values of two samples separated by a 15 min. interval were found to agree within ± 2 per cent with those derived from three or more samples.

In the great majority of injured patients, with wounds of widely differing extent and with varying circulatory states, the rate of dye loss estimated from the fall in dye concentration over 30 to 45 min. varied between 5

and 12 per cent of the total per hour In a few cases, about 8 per cent of over 200 plasma volume estimations, it was between 15 and 20 per cent for the first hour, but these rates may have been exaggerated by small errors in estimation or by the shortness of the periods during which samples were drawn Loss of the order of 30 per cent or more of the total in the first hour was never encountered

Determination of Blood Volume and Red Cell Volume

Blood volume was calculated from the formula

$$\text{Blood volume} = \text{plasma volume} \times \frac{100}{100 - \text{haematocrit}}$$

The haematocrit was not corrected for trapped plasma

The red cell volume was determined from the formula

$$\text{Red cell volume} = \text{blood volume} - \text{plasma volume}$$

TABLE 39

Blood and red cell volume in 25 near-normal front line troops

Subject	Age	Height (in)	Red cell volume (ml)	Total blood volume (ml)
1	25	72	3190	7050
2	22	69	2940	6260
3	25	65	2160	4430
4	31	67	2590	5550
5	34	64	2580	5200
6	25	64	2920	5640
7	25	71	2940	6100
8	41	66	2680	5810
9	24	66	2200	4820
10	33	72	2760	6000
11	20	72	2840	6520
12	25	71	3010	6020
13	27	70	2600	5660
14	33	71	3240	6740
15	23	66	2420	5200
16	36	66	2320	5090
17	21	72	3250	6480
18	28	65	2380	5060
19	26	69	2360	5360
20	23	69	2670	5450
21	32	66	3140	6240
22	33	69	2820	5970
23	44	66	2690	5980
24	25	69	2820	6020
25	25	71	2650	5520

"Prediction" of Normal Blood Volume and Normal Red Cell Volume

It has been shown that normal blood volume and red cell volume are fairly closely related to height and weight and hence can be predicted from either or both of these measurements Most British front line soldiers did not know their weight, nor, once they were injured, bandaged and splinted,

could they be weighed. Their normal blood volumes were therefore predicted from their measured heights, using values obtained from Figure 8 of Gibson and Evans (1937),* and their normal red cell volumes from these blood volumes, assuming a haematocrit of 47 per cent. These values, hereafter called "predicted normal" values, have been compared with those measured in 25 near-normal front line troops who were either suffering from minor wounds, from which it is certain that they had lost little blood, or recovering from minor illnesses. In Table 39 are given the details of the blood volume estimates on these troops. In Table 40 (A) are shown the "predicted normal"

TABLE 40

Blood and red cell volume in fit adult men, related to height

Height (in.)	A		B	
	Blood volume (ml.)	Red cell volume (ml)	Blood volume (ml.)	Red cell volume (ml)
63	4460	2100	4910	2390
64	4800	2260	5065	2455
65	5000	2350	5215	2520
66	5200	2440	5370	2580
67	5340	2510	5520	2645
68	5480	2570	5675	2710
69	5560	2610	5830	2775
70	5660	2660	5980	2840
71	5720	2690	6135	2900
72	5800	2730	6290	2965

A shows the values used in the report for predicting normal volumes from height The blood volumes were obtained from Fig 8 of Gibson and Evans (1937), the red cell volumes by multiplying these blood volumes by 0 47

B shows values calculated from linear regression equations, derived from the data of Table 39

Blood volume = 5720 + 153 (H−68 3) ml
(Standard error of regression coefficient ± 34)

Red cell volume = 2730 + 64 (H−68 3) ml
(Standard error of regression coefficient ± 19 7)

where H is the measured height in inches.

blood volume and red cell volume obtained from height as described, and in 40 (B) the figures obtained from the regression equations relating height to blood volume and to red cell volume from the data in Table 39.† From a comparison of columns A and B it is clear that the "predicted normal" values are conservative in size, blood volumes in column A being 3–10 per cent smaller than those in column B. The choice of subjects on whom the blood volume and red cell volume estimations were made in Table 39 was fortuitous, and it is probable that these subjects form a reasonably fair sample of British front line troops.

*When it has been obvious in a few unusually thickset and muscular individuals that the normal blood volume so calculated was much too low, the estimate has been increased by 10 per cent

†I am much indebted to E. C Reeve for the statistical analysis shown in this section

The probable variation in blood volume and red cell volume that will be found for a given height can be obtained thus (Fisher, 1946, § 26)

The variance of blood or red cell volume (V) for a particular height is given by the equation

$$V = S^2\left(\frac{1}{n} + \frac{(H - \bar{H})^2}{\Sigma(H - \bar{H})^2}\right)$$

where S^2 = mean square of differences between actual values and values predicted by regression equations,
n = number of blood volume or red cell volume estimations,
H = any given height,
$\bar{H}$ = mean height

Having determined V for a particular height and writing "normal deviation" $= t \times \sqrt{V}$, from Fisher's table (Fisher, 1946) one can determine the value of t which will include a desired proportion of the population For the data shown in Table 39 t will exceed 1 714 in 10 per cent of cases, of which 5 per cent will be extreme deviations above the average and 5 per cent extreme deviations below

Using these equations, from the data of Table 39 one can calculate that at mean height (68 3 in) 90 per cent of the values of blood volume should lie between (predicted value $\times$ 1 14) and (predicted value $-$ 1 14) and 90 per cent of the values of red cell volume should lie between (predicted value $\times$ 1 17) and (predicted value $-$ 1 17)

If the small increase in tolerance which must be made at the extremes of the height scale is neglected, in the majority of cases the blood volume estimate will be within $\pm$ 15 per cent of the value shown for a particular height in column B of Table 40, and the red cell volume estimate within $\pm$ 20 per cent of the value shown

METHOD OF ESTIMATING HAEMORRHAGE

In man there is little evidence of appreciable quantities of stored red cells in the body and it is known that lost red cells are replaced only slowly So if a man's initial volume of red cells is known, and if the volume left after bleeding can be determined, then the difference between these two amounts is proportional to the blood lost Supposing for instance a man before haemorrhage had 2,500 ml , and after haemorrhage 1,500 ml., of red cells, then he has lost blood containing 1,000 ml of red cells, or 40 per cent of his original blood This method of estimating haemorrhage has been used here for lack of a better, though as will be seen it is only approximate

VALUE AND MEANING OF ESTIMATIONS

In the foregoing pages various circulatory states have been related to estimates of blood volume as percentage of normal volume,

$$\frac{\text{Estimated blood volume} \times 100}{\text{Predicted normal blood volume}},$$

and to estimates of percentage blood loss from the formula

$$100 - \frac{\text{Estimated red cell volume} \times 100}{\text{Predicted normal red cell volume}}.$$

To discover whether these are true estimates it is necessary to assess the accuracy both of the predicted normal values and of the post-injury estimates. The accuracy of prediction and of post-injury estimates made during normal circulatory states can be assessed, but at present there is too little information for precise assessment to be made during abnormal circulatory states. But it will be seen that the balance of the evidence is that the estimates of reduction in blood volume and of haemorrhage are of the right order.

Accuracy of "Prediction" of Normal Values

It has already been noted that in the great majority of cases the blood volume predicted from height will lie within $\pm$ 15 per cent, and the red cell volume predicted from height within $\pm$ 20 per cent, of the values shown in column B of Table 40. But the actual values used for prediction, shown in column A of Table 40, are 3–10 per cent less than those shown in column B. Hence in the average case the predicted blood volume and red cell volume will be 3–10 per cent less than the probable volumes. It will be seen that this underprediction has advantages in counteracting possible overestimates of blood loss and changes in blood volume in patients who have lost much blood.

Truth of Dye Haematocrit Estimates

Normal Subjects

In dye methods the volume of plasma is determined by the dilution of a known quantity of dye in the plasma, from the equation $V = \frac{N}{n}$, where V = plasma volume, N = the total quantity of injected dye and n = the quantity of dye in unit volume of plasma. Excluding errors of estimation, the estimate of V can only be in error if the injected dye is unevenly distributed through the plasma, or if part of the injected dye is lost from the circulation and no correction is made for this loss. In normal subjects it seems probable that values of V obtained by the methods here used approach close to the true plasma volumes; for evidence for this statement see Barnes *et al.* (1948) and Reeve (1948). The best estimate of true red cell volume is obtained with a reliable marked red cell dilution method, and the best estimate of true blood volume by adding this estimate to the dye plasma volume estimate. Comparing the dye haematocrit estimates of red cell volume $\left(= \text{plasma volume} \times \frac{\text{haematocrit}}{100 - \text{haematocrit}}\right)$ and of blood volume $\left(= \text{plasma volume} \times \frac{100}{100 - \text{haematocrit}}\right)$ with these best estimates shows that on the average in normal subjects the dye haematocrit estimate of red cell volume is about 25 per cent too great, and that of blood volume about 10 per cent too great (Reeve, 1948). This overestimate is due first to error in the haematocrit, when the haematocrit is spun with a force of 1,500 $\times$ gravity for 30 min.,

as in these observations, about 5 per cent of the packed red cell column consists of trapped plasma, so that the true dye estimate of red cell volume should be

$$\text{Dye plasma volume} \times \frac{0\,95 \times \text{haematocrit}}{100 - 0\,95 \times \text{haematocrit}},$$

which in normal subjects results in an 8–10 per cent smaller estimate of red cell volume than the conventional estimate In normal subjects even this corrected formula gives about a 15 per cent overestimate of red cell volume and about ■ 6 per cent overestimate of blood volume This overestimate might be due to (*a*) undetected dye loss from the plasma, or (*b*) varying distribution of red cells and plasma in different parts of the circulation There is no evidence of (*a*) but definite evidence of (*b*), and it seems probable that the dye corrected-haematocrit overestimate of red cell volume is mainly due to a greater proportion of plasma to red cells in the minute vessels than in the larger vessels The evidence for the above statements will be found in Barnes, Loutit and Reeve (1948) and Reeve (1948)

Injured Subjects

To relate the dye haematocrit estimates of red cell and blood volume to estimates of true red cell and blood volume in the various disturbed circulatory states described in the foregoing pages would require many careful balance experiments using dye and marked red cell dilution methods In man such experiments are difficult and have not been made, and only a few have been made in animals However, it is still possible in man to examine what effects are likely to occur and to apply the findings of animal experiment. Such an examination will display the errors to which dye estimates of plasma, red cell and blood volume in such disturbed states of the circulation may be subject

The most pronounced circulatory disturbances are seen in patients with gross injuries and much blood loss, who show marked vasoconstriction with diminished cardiac output and diminished blood flow through the skin, muscles and viscera No attempt, as has already been noted, was made to estimate blood volume in such patients who were critically ill, but estimations were made on those showing smaller degrees of circulatory disturbance

Generalized vasoconstriction must result in (i) slower mixing of an injected dye through the plasma, and (ii) reduction of the calibre of the blood vessels

Incomplete mixing of dye through the plasma Zweifach, Lee, Hyman and Chambers (1944) have reported that direct observation of the small vessels of the omentum of dogs, subjected to considerable haemorrhage and maintained with low blood pressures, shows areas of circulatory stasis Gibson, Seligman *et al* (1947) report that, when five dogs were bled of 35–50 per cent of their total blood, injected marked red cells failed to mix with 4–20 per cent of the initially estimated total red cells, and injected T1824 failed to mix with 1–7 per cent of initially estimated total plasma volume These experiments indicate that when there is pronounced vasoconstriction a proportion of the circulation may not be reached, or may only slowly be reached, by injected dye or marked red cells *Few details of the circulatory states of the experimental*

animals are given, but three out of five were probably near or in the condition thought in man to be too serious for blood volume estimates to be attempted. From these experiments it seems probable that in patients with gross circulatory disturbance a portion of the circulation may not be reached by injected dyes. In the patients with the greatest circulatory disturbance here studied it seems improbable that more than 10 per cent of the initial circulatory volume was so cut off.

If injected dye fails to reach all the intravascular plasma and is distributed only through the more rapidly flowing portion, plasma volume, and hence red cell and blood volume, will be underestimated, and the estimates of blood volume reduction and haemorrhage will both be too great.

Reduction in calibre of the blood vessels. In the injured patient suffering from marked circulatory disturbance the size of the dye haematocrit overestimate of red cell volume, which in normal subjects is about 25 per cent, is at present uncertain. The most probable cause of variations in its size is alteration in the proportions of plasma to red cells with alteration in the calibre of the blood vessels. The effects of such changes can be shown thus. For simplicity assume that the haematocrit per cent red cell concentrations are corrected to true values, and call such corrected values H. Then the dye corrected haematocrit estimate of red cell volume (R.C.V.) becomes P.V. $\times \dfrac{H}{100 - H}$, where P.V. is plasma volume. Give a value to "plasma volume A" (P.V.A.) such that P.V.A. $\times \dfrac{H}{100 - H}$ = true R.C.V. In normal subjects $\dfrac{\text{P.V.A.}}{\text{total P.V.}}$ averaged 0·87 (Barnes *et al.*, 1948). P.V.A. is, by definition, the volume of plasma distributed with the total red cell volume in the proportions of the observed corrected haematocrit. The difference between total plasma volume and P.V.A. may be called "plasma volume M" (P.V.M.). In the absence of evidence to the contrary P.V.A. may be regarded as the "axial plasma" and P.V.M. as the "marginal plasma". The marginal plasma may tentatively be regarded as the plasma lining the internal surfaces of the vessels, chiefly the minute vessels. For a constant size of overestimate of red cell volume by the dye method the ratio $\dfrac{\text{P.V.A.}}{\text{total plasma volume}}$ and hence also $\dfrac{\text{P.V.M.}}{\text{total plasma volume}}$ must remain constant. If the latter ratio decreases there will be a smaller overestimate, if it increases there will be a greater overestimate.

That it does increase in cases of circulatory disturbance is suggested by a series of 28 simultaneous measurements of red cell volume made by Gibson, Seligman *et al.* (1947) in dogs in varying degrees of shock Two methods were used, radioactively marked red cells, and T1824/haematocrit. The auricular haematocrits ranged from 19 to 69 and averaged 43·7, and on the average the dye haematocrit method gave a red cell volume overestimate of 32 per cent. In normal dogs the overestimate was 20 per cent. If these results can

be applied to man they indicate that in subjects with low blood pressure and vasoconstriction the dye haematocrit method would tend to give a greater overestimate of total red cell volume and of blood volume—i e that $\frac{\text{P V M}}{\text{total plasma volume}}$ would be higher—than in subjects whose circulation was normal

Combined Effects of Various Errors on Estimations of Haemorrhage and Blood Volume Reduction

In Table 41 are shown, in three typical patients (*I* 78, *I* 99 and *I* 104), the errors that a low predicted normal red cell and blood volume, incomplete distribution of dye through the plasma, and an increased proportion of blood with a lower haematocrit in the minute vessels might be expected to introduce into estimates of size of blood volume and amount of blood loss For each patient three groups of values are shown, Group A, the predicted normal red cell volume, plasma volume and blood volume, Group B, the measured post-injury red cell volume, plasma volume and blood volume and Group C, the values of Group B expressed as percentages of those of Group A The working of the table for the first patient, *I* 78, is illustrated The predicted normal pre injury values shown in column (1) A are those predicted from height as earlier described They are derived from plasma volume measured by dye, and red cell volume determined from the plasma volume and haematocrit uncorrected for trapped plasma Column (1) B shows the values measured after injury by the dye method, again with the haematocrit uncorrected In column (1) C are shown the values of column (1) B expressed as percentages of the predicted normal of column (1) A In Part I, this patient at the time of the measured blood volume is taken as having a blood volume of 60 per cent normal and a red cell volume of 49 per cent normal, i e he is taken to have lost by haemorrhage almost 50 per cent of his initial blood, but to have increased his plasma volume by dilution At the time of the blood volume estimation the patient, whose left foot had been blown off by a mine 3½ hr before, had not been transfused, he was conscious, anxious, alert, his pulse rate was 130, his blood pressure 70/60, respirations were sighing and extremities cool, but the veins were not markedly constricted, and there was no difficulty in obtaining blood samples

On the average the red cell volumes in normals measured by the dye method with the uncorrected haematocrit are about 25 per cent too high In column (2) A is shown the "true" normal red cell volume, which is the predicted normal of column (1) A divided by 1 25 The "true" normal blood volume now becomes the sum of this new value for red cell volume and the predicted normal plasma volume, these values also are shown in column (2) A

Earlier it has been stated that it is probable that the dye method gives an even greater overestimate of red cell volume after considerable blood loss than in normal subjects It is here assumed to be of the order of + 35 per cent, and to obtain the "true" red cell volume after injury the observed value of column (1) B must be divided by 1 35, giving the figure shown in column (2) B Thus added to the observed dye plasma volume will give the estimated

TABLE 41

Illustrations from patients of possible magnitude of errors in estimating blood volume reduction and haemorrhage

	(1) Estimates as used			(2) Red cell volumes corrected for overestimate by dye haematocrit method			(3) Red cell and blood volumes corrected for shut-off portions			(4)	
	A Predicted normal T 1824/ haematocrit (ml)	B Measured post-injury T 1824/ haematocrit (ml)	C Measured post-injury as per cent of 1A	A Predicted normal R C V – 1 25 (ml)	B Measured post-injury R C V – 1 35 (ml)	C Measured post-injury as per cent of 2A	A Predicted normal (as 2A) (ml)	B Post-injury add 10 per cent of values of 2A to values of 2B	C Post-injury as per cent of values of 3A	Limits of predicted normal values in 90 per cent of troops	Clinical Notes
I 78											Aet 24 Conscious, anxious, alert Pale, cool extremities Low venous pressure in neck Sighing respiration No transfusion Blood volume estimated 3½ hr after injury Mine wound traumatic amputation left foot with 2 hands muscle damage
R C V	2600	1270	49	2080	940	45	2080	940+210	55	2750±450	
P V	2920	2060	70	2920	2060	70	2920	2060+290	80	3000	
B V.	5520	3330	60	5000	3000	60	5000	3000+500	70	5750±750	
I 99											Aet 21 Mentally clear Cold extremities, very pale. Pulse rate 112 Blood pressure 100/70 No transfusion Blood volume estimated about 6 hr after injury Fainted on way to C C S Mine wound both feet badly crushed and disorganized, muscles of lower half of one leg shattered
R C V	2660	1410	53	2130	1040	49	2130	1040+210	59	2840±470	
P V	3000	2070	69	3000	2070	69	3000	2070+300	79	3140	
B V	5660	3480	62	5130	3110	60	5130	3110+510	70	5980±800	
I 104											Aet 25 Drowsy (morphine), thirsty Cool extremities. Pulse rate 100 Blood pressure 115/80 Blood volume estimated 3½ hr after injury No transfusion Mine wound traumatic amputation left foot and leg, compound fracture lower right tibia and fibula, anterior tibial artery torn (See p 55)
R C V	1970	1510	77	1580	1120	71	1580	1120+160	81	2320±460	
P V	2230	1850	83	2230	1850	83	2230	1850+220	93	2430	
B V	4200	3360	80	3810	2970	78	3810	2970+380	88	4750±750	

R C V = red cell volume P V = plasma volume B V = blood volume

actual blood volume In column (2) C are shown the values of column (2) B expressed as percentages of column (2) A These percentages may be compared with those shown in column (1) C It will be noted that, whereas there is no change in the estimate of the percentage reduction of blood volume, the estimate of blood loss is even greater, 55 per cent instead of 51 per cent

In men suffering from much blood loss it is possible that as much as 10 per cent of their initial blood is not reached by an injected substance The values given in column (2) B may be regarded as referring to the volume of actively circulating red cells and plasma In column (3) B are calculated the total red cell volume and plasma volume contained in the circulation on the assumption that after injury 10 per cent of the intial true red cell volume and plasma volume are in very slow circulation It should be noted that 10 per cent of the initial blood volume is a considerably higher proportion of the blood volume remaining after haemorrhage, e g 20 per cent if half the blood has been lost in external haemorrhage The normal values for red cell volume, plasma volume and blood volume shown in column (3) A are the same as those in column (2) A In column (3) C are shown the values of (3) B plotted as percentages of (3) A It can be seen that all values in column (3) C have increased by 10 per cent and that the true blood volume is 70 per cent where the circulating volume was 60 per cent Since a true estimate of external haemorrhage must be based on a measure of all the red blood cells contained in the circulation, haemorrhage is now estimated to have been 45 per cent, not 55 per cent

It will be noted that the effects of an increase in the ratio $\frac{\text{P V M}}{\text{total plasma volume}}$ on the one hand, and are stagnant flow on the other, in opposite direction

In column (4) are shown for patients of the height of *I* 78 the mean value and the range which includes 90 per cent of normals taken from the series of blood volume estimations on troops shown in Table 39 It will be seen that the predicted normal red cell volume of column (1) A is 5 per cent lower than the mean normal of column (4) Taking values at the lowest end of the normal ranges shown in column (4), the predicted normal blood volume is unlikely to be more than 10 per cent too great and the predicted normal red cell volume is very unlikely to be more than 12 per cent too great When dealing with the results on a number of patients the probability is that the average prediction of the initial dye plasma volume and the dye red cell volume will be too small This will counteract the possible overestimate due to stagnant portions of the circulation in those with large and very large injuries

In Table 41 are shown similar predicted, estimated and calculated red cell volumes, plasma volumes and blood volumes for two other injured patients for comparison with patient *I* 78 Patient *I* 104 is included, not because he suffered from a gross reduction of blood volume and red cell volume, but because, despite very large injuries he did not

As a summary to this section the effects of the various factors influencing the estimate of blood and red cell volume reduction by the dye haematocrit method are set out in Table 42 It can be seen that the greatest errors in

TABLE 42

Factors affecting the accuracy of estimates of reductions in blood volume and losses of red cells derived from T1824/haematocrit estimates of blood and red cell volume: a summary

1.	In unwounded subjects the T1824/haematocrit method used in this work gives a true estimate of plasma volume, about a 25 per cent overestimate of red cell volume, and hence about a 10 per cent overestimate of blood volume
2	Were the method to give identical overestimates of red cell (R.C V) and blood volume (B V.) in the disturbed circulatory states occurring after much haemorrhage, then estimates of the percentage red cell losses as $100 - \dfrac{\text{measured post-injury R.C V} \times 100}{\text{measured pre-injury R C V.}}$ and of the percentage reduction in blood volume as $\dfrac{\text{measured post-injury B V} \times 100}{\text{measured pre-injury B V.}}$ would be nearly true
3.	But it cannot be safely assumed that this is so Two factors, separately or combined, may reduce the size of the overestimate, or even turn it into an underestimate. (*a*) Because of slowed circulation, injected T1824 may fail to reach all the plasma Too low a plasma volume, and hence too low a red cell and blood volume (in the terms of the method) will then be measured (*b*) A change in distribution of the red cells and plasma in the circulation may alter the size of overestimate of red cell volume, e g from the usual overestimate of × 1 25 to × 1 35 Increase in the overestimate will tend to reduce errors caused by 3 (*a*) and decrease to increase them. However, when there has been much loss of red cells, factor 3 (*b*) by itself will not greatly throw out percentage estimates of red cell loss and blood volume reduction.
4	Also, the blood and red cell volume before injury cannot be measured and must be "predicted". If values are predicted too high, too great a reduction in blood volume and loss of red cells will be obtained To lessen the chances of such an error and to counteract errors arising from 3 (above) normal values were predicted 3–10 per cent lower than those found by measurement in forward troops
5	Illustrations of the possible magnitude of the errors resulting from underestimating post-injury plasma volume, from post-injury alterations in the distribution of cells and plasma, and from "predicting" pre-injury blood volume, are given in Table 41.

estimates of change in blood volume and haemorrhage will be caused by a combination of (i) failure of injected dye to mix with all the plasma, and (ii) reduction of the overestimate of the red cell volume given by the dye haematocrit method.

Tests of Estimates

Blood Loss

From what has been said it will be apparent that estimates of haemorrhage derived from estimates of red cell volume are more likely to be considerably in error than estimates of reduction of blood volume. In injured men it is rarely possible to compare an estimate of haemorrhage with the measured blood loss, for in the majority of cases blood is lost externally and into bruised tissue and thus cannot be measured. But in two patients suffering from wounds of the abdomen (*B*.32 and 71), and in one patient (not in this series) who suffered from a ruptured ectopic pregnancy, this comparison could be made, since much or all of the blood lost had collected in their peritoneal cavities and could be removed and measured. Details of these three patients

TABLE 43

Test of methods for measuring haemorrhage

Patient	Injuries	Clinical condition			Previous transfusion	Measured blood and red cell volumes			Estimated blood loss (per cent *normal* blood volume)	Blood found in abdomen	
		Pulse rate	Blood pressure	General			ml	Per cent normal		ml	Per cent normal blood volume
B 71	Penetrating abdominal wound, two perforations of stomach, bruising of gastro-colic omentum, perforation of transverse colon, gastro epiploic vessels torn in two places, small wound in right leg with torn vessels	128	*95/60*	*Cold extremities, pale face*	One bottle of blood	B V	3160	68	50	2350	45
					Two bottles of plasma	R C V	1110	51		Bleeding may have occurred between estimation and collection	
(pp 125 and 147)						*Measured 5¼ hr after injury*					
B 32	Through and through abdominal wound, penetrating wounds of stomach, hole in pancreas, renal pedicle, including branches of renal artery, torn, retroperitoneal haematoma	106	85/70	Cool extremities	One bottle of blood	B V	3590	72	45	1400	30
						R C V	1340	57		Also large retroperitoneal haematoma	
(p 173)						Measured 2¼ hr after injury					
Not dealt with in this report	Ruptured ectopic pregnancy					B V	2320	60			
						R C V	700	45	55	2020	52

and a comparison between the estimated and the measured blood losses are shown in Table 43. In the two patients suffering from penetrating abdominal wounds, blood lost externally or into the tissues is not included in the measured blood loss. It can be seen that agreement between estimated and measured haemorrhage is reasonably good. Ebert and Stead (1941) give protocols of experiments in which dye haematocrit estimates of plasma and red cell volume were made on men before and after measured bleedings of up to 20 per cent of the total blood volume. From the figures given, a fairly good estimate of these subjects' normal true red cell volume may be calculated. Summing these values and the estimated plasma volumes gives the true normal blood volumes, and the true percentage haemorrhage is then calculated as

$$\frac{\text{measured volume of blood removed} \times 100}{\text{true normal blood volume}}$$

These values may be compared with estimates of percentage haemorrhage made by the dye uncorrected-haematocrit method from the formula

$$100 - \frac{\text{dye haematocrit red cell volume (after haemorrhage)} \times 100}{\text{initial dye haematocrit red cell volume}}.$$

Such comparisons are shown in Table 44 and it can be seen that with these smaller haemorrhages the dye haematocrit method gives a fairly close estimate of true haemorrhage. Stead and Ebert (1941) report dye haematocrit estimates before and after repeated large haemorrhages in dogs. In these experiments the dye haematocrit method appeared to give a 20 per cent or greater overestimate of red cells lost. It is difficult to reinterpret these experiments in terms of the truth of the estimate of percentage loss of red cells, but it seems that the dye haematocrit method may give a 10 per cent overestimate of haemorrhage.

Blood Volume

There has been so much criticism of dye methods of estimating blood volume that here we give some evidence that on repetition in injured patients they give reasonable results.

Noble and Gregersen (1946b) give observations on five patients suffering from haemorrhage and low blood pressure. With the dye haematocrit method, total red cells and total plasma protein were estimated before and after transfusion of known amounts of red cells and plasma protein. The differences between the first and second dye haematocrit estimates agreed fairly well with the measured quantities of red cells and protein transfused.

Emerson and Ebert (1945) present in Table 2 of their paper a number of repeated estimates of plasma volume and haematocrit, separated by intervals of 2½–9 hr. and made on battle casualties given considerable pre-operative transfusions of dilute blood and plasma. The methods of estimation were comparable with ours, and the second estimation was made within 10–30 min. of cessation of the transfusion. Transfusions ranging in total volume between 2,250 and 5,500 ml. were given over periods varying from 2½ to 9 hr. The average rate of transfusion was about 1,000 ml. per hour, but in some this rate was doubled. Thus in these cases the second estimate of blood volume was made

TABLE 44

Comparison of dye uncorrected haematocrit estimates of haemorrhage with measured blood loss, from data of Ebert and Stead (1941) *in part recalculated*

Patient	Initial true red cell volume (ml)*	Initial dye haematocrit estimate of red cell volume (ml)	Second dye haematocrit estimate of red cell volume		Third dye haematocrit estimate of red cell volume		First and second dye/haematocrit estimates of blood withdrawn (per cent initial blood volume)†		Measured blood withdrawn (per cent true initial blood volume)‡
			ml	Time after bleeding	ml	Time after bleeding	(1)	(2)	
J C	2190	2770	2340	36 min	2360	6 hr 48 min	15	15	21
R C	1810	2280	1860	45 min	1790	7 hr 40 min	18	21	17
J F	1940	2440	1950	4 hr 45 min		—	20	—	20
M K	1770	2230	1810	1 hr 50 min	1710	23 hr	19	23	22
T W	2400	3020	2210	6 hr 10 min	2165	24 hr	27	28	20
A B	1810	2280	1730	5 hr 30 min		—	24	—	18
							Mean 21		Mean 20

* Estimated as $\left(0.87 \times \text{initial dye plasma volume} \times \dfrac{0.95 \times \text{haematocrit}}{100 - 0.95 \times \text{haematocrit}}\right)$

† Estimated as $\left(100 - \dfrac{\text{2nd or 3rd dye haematocrit red cell volume} \times 100}{\text{initial dye haematocrit red cell volume}}\right)$

‡ Estimated as $\left(\dfrac{\text{measured blood withdrawn} \times 100}{\text{initial plasma volume} + \text{initial true red cell volume}}\right)$

after very considerable transfusion, which would be expected to cause considerable fluctuations in the circulation because of rapid fluid exchanges, alterations in blood pressure and blood flow, and the pharmacological effects of the transfused fluids. Data for those of their cases that were comparable with those dealt with in this report are presented in Table 45, in which are shown details of the injuries, of the first and second estimates of blood volume, total red cell volume and total plasma protein, and of the volume of red cells, the volume of fluid, and the total protein transfused. From these data, balances are calculated to show what amounts of transfused red cells, protein and fluid appeared to leave the circulation, as determined from the difference between the first and second blood volume estimates. Allowing as error of the methods used $\pm$ 200 ml. red cells and $\pm$ 20 g. protein, it will be seen that in limb cases *E*.12 and *E*.48 and in abdominal cases *E*.2, *E*.14, *E*.16, *E* 21, *E*.23 and *E*.39 the balances of red cells and plasma protein are satisfactory as indicating differences not greater than would reasonably be expected from the errors of the methods and imperfections of the fluids transfused. This provides strong additional evidence that the methods of estimating plasma and red cell volume used under such testing circumstances in battle casualties give estimates of the right order. Limb cases *E*.9, *E*18, *E*.19 and *E*.31 and abdominal cases *E*.1, *E*.11 and *E*.47 show negative balances of transfused red cells and/or protein beyond the limits of error allowed; however, in cases *E*.1 and *E*.47 they are very near those limits. In *E*.11, the other abdominal case, they are probably due to leakage of plasma, and in the limb cases to losses of whole blood and plasma into damaged tissues. The high ratio of lost red cells to plasma protein in *E*.31 suggests also the removal of imperfectly stored red cells. The data shown in Table 45 are of considerable interest since the second blood volume estimates were made under circumstances (i.e. after great or rapid transfusion) that we avoided, as we noted earlier, because of the greater risks of errors in the methods.

Some of our own findings are summarized in Table 46. In Section A are shown repeated red cell volume and total plasma protein estimates on three patients suffering from minor injuries (*Cases I*.1, *I*.2 and *I*.9). Between the two estimates there was an interval of 3½–4 hr. during which each patient underwent operation, but lost a negligible amount of blood. It can be seen that the first and second estimates agree within the errors of the method: thus operation and anaesthetic do not of themselves alter such estimates. In Section B of the table similar repeated estimates, separated by intervals of 2½–5 hr., are shown for four untransfused patients (*Cases I*.41, *I*.49, *I*.79 and *I*.88) who suffered from moderate or large injuries. Again, each patient underwent operation in the interval between the two estimates, and at operation all blood lost externally was collected so far as possible and its volume estimated from measurement of its total haemoglobin content. It can be seen that in *Cases I*.79, *I*.49 and *I*.88 there was an estimated decrease in total red cells and protein rather greater than was to be expected if the estimated blood loss was the only blood leaving the circulation. However, there was opportunity during and after operation for further unmeasured blood loss.

TABLE 45

Balance table taken from observations of Emerson and Ebert (1945)

Patient	Injuries	Transfusion between first and second blood volume estimates: Red cells (ml)	Plasma protein (g)	Fluid (ml)	Interval between first and second blood volume estimates (hr)	Estimates a—first b—second	Haematocrit (per cent)	Plasma protein (g per 100 ml.)	Blood volume (ml.)	Red cells (ml)	Plasma protein (g)	Balance: Red cells (ml)	Plasma protein (g)	Fluid (ml)
	Patients with Limb Injuries													
E 9	Compound fracture of humerus mandible and zygoma	1000	105	3250	8½	a	38 5	5 1	3450	1320	109	−320	−31	−1930
						b	36 7	5 3	5450	2000	183			
E 12	Traumatic amputation of leg perforated caecum	900	87	1850	6	a	27 6	5 9	2340	680	98	−30	+13	−310
						b	32 6	6 2	4750	1550	198			
E 18	Gunshot through axilla severing brachial artery and vein	750	87	2750	5	a	27 4	5 9	3030	830	130	−290	−53	−2080
						b	31 0	5 8	4160	1290	164			
E 19	Compound fracture of humerus scapula and clavicle	750	81	2700	4	a	33 7	6 2	3420	1190	138	−420	−33	−1550
						b	31 0	5 5	4900	1520	186			
E 31	Compound fracture of humerus scapula and clavicle	1150	98	3700	4	a	38 1	6 0	4030	1540	149	−710	−32	−2670
						b	36 0	6 1	5500	1980	215			
E 48	Mine wounds compound fracture of right femur right and left tibiae right radius	1170	82	2630	4	a	24 2	5 4	2390	580	98	−120	−14	−1060
						b	32 6	4 9	5010	1630	166			
	Patients with Abdominal Injuries													
E 1	Perforations of rectum colon and small intestine	1250	105	4000	2½	a	41 5	6 3	3810	1580	140	−220	−25	−2570
						b	41 6	6 0	6270	2610	220			
E 2	Laceration of colon and kidney	1000	87	3250	3½	a	32 4	5 3	3610	1170	129	+80	−4	−1690
						b	36 0	5 3	6250	2250	212			
E 11	Perforations of colon liver gall bladder and duodenum	1000	98	3400	5	a	32 1	6 5	2450	790	108	−280	−52	−2310
						b	35 5	5 6	4260	1510	154			
E 14	Multiple perforations of colon and small intestine compound fracture of tibia	1000	87	3250	3	a	32 8	5 8	3230	1060	126	+60	+1	−1740
						b	36 5	5 8	5800	2120	214			
E 16	Perforation of duodenum and inferior vena cava	1000	105	3500	3	a	31 8	6 4	3160	1000	138	−50	+4	−1860
						b	34 0	6 5	5750	1950	247			
E 21	Lacerated liver	500	53	1750	6	a	39 6	7 3	4270	1690	188	+80	+5	−950
						b	40 2	7 3	5650	2270	246			
E 23	Lacerated liver and kidney compound fracture of femur	1000	88	3250	6½	a	35 4	6 9	2840	1010	126	+80	−2	−1660
						b	38 0	6 2	5510	2090	212			
E 39	Multiple perforations of small intestine and colon	1250	105	4000	3	a	26 4	5 4	2520	670	100	+110	−12	−2580
						b	39 2	5 9	5300	2030	193			
E 47	Multiple perforations of small intestine compound fracture of right ilium	1250	122	4250	9	a	37 0	5 8	2920	1080	107	+130	−29	−2820
						b	43 0	6 1	5730	2460	200			

Note To distinguish *these cases* from our own the letter E has been prefixed to the case numbers given by Emerson and Ebert

TABLE 46

Repeated dye haematocrit estimates of red cell volume and total plasma protein in injured patients

Patient		Injuries	First estimate of red cell volume (ml.) and total plasma protein (g.)	Interval between two estimates (hr.)	Second estimate of red cell volume (ml.) and total plasma protein (g.)	Clinical notes of period between the two estimates (including operation)
A	*I.2*	Minor	3010 ml. 206 g.	3½	2970 ml. 196 g.	General state good, short operation with minimal blood loss and manipulation, anaesthetic 1·3 g. "Pentothal"
	I.1	Minor	3240 ml 209 g.	4	3270 ml. 210 g	As above, 1 75 g. "Pentothal"
	I 9	Multiple minor	2760 ml. 202 g.	4	2860 ml 214 g.	As above, 15 ml ethyl chloride, 8 oz. ether by Oxford vaporizer
B	*I.41*	Mine wound: traumatic amputation of right foot through ankle joint with 1 hand muscle damage	2470 ml 175 g Blood volume 102 per cent predicted normal	2½	2400 ml. 173 g.	General state good; anaesthetic 2·3 g "Pentothal", amputation through lower third of leg; 120 ml. measured blood loss at operation, no transfusion
	I.79	Mine wound right foot disarticulated at ankle, at least 2 hands muscle damage in lower half right leg	1520 ml 149 g. Blood volume 70 per cent predicted normal	3½	1220 ml 131 g.	Pre-operative pulse rate 100–120, blood pressure 140/80, pale, no marked vasoconstriction; operation 1 hr; difficult anaesthetic ("Pentothal" and trilene), amputation through upper third of leg; post-operative fall of blood pressure and rise of pulse rate, at 2nd blood volume estimate, pulse rate 124, blood pressure 70/45, no transfusion, measured external blood loss at operation 250 ml
	I.49	Small wound of foot; compound fracture of right femur with considerable swelling of upper third of thigh	1500 ml. 166 g Blood volume 84 per cent predicted normal	3½	1170 ml 143 g	Pre-operative pulse rate 130, blood pressure 125/70, pale, warm extremities, at operation, long incisions made in thigh, which was plastered, ethyl chloride induction and ether by Oxford vaporiser, bronchoscopy at end of operation, measured external blood loss at operation 340 ml., no transfusion; plasters blood-stained after operation
	I 88	Mine wound: right foot shattered and calf muscles considerably damaged	1800 ml. 142 g Blood volume 80 per cent predicted normal	5	1550 ml. 132 g.	Pre-operative pulse rate 76, blood pressure 135/80; pale, cool extremities, at operation, amputation above knee under 2 4 g. "Pentothal"; measured operative external blood loss 300 ml, bleeding from amputation stump after operation; no transfusion

Comment

From the foregoing discussion it can be seen that the dye method as here used cannot at present be claimed to give precise measurements of blood and red cell volumes, or of changes in these volumes, in injured patients This is chiefly due to lack of information on the errors to which it is subject in abnormal circulatory states However, for the understanding and correct management of injured patients very precise estimates are not required, it is sufficient if they are of the right order, and the examination made above of errors suggests that this is so Further, there is strong independent clinical evidence to the same effect Thus at first we were inclined to disregard estimates that did not tally with our clinical impression—for example, if a patient was thought to have been sufficiently transfused and a blood volume estimate then seemed to show that he had much reduced volumes of blood and red cells, this estimate was disregarded, but experience showed that when such patients were further transfused their circulatory states and clinical condition showed striking improvement So with greater experience we tended to give the amounts of transfusion indicated by the results of blood volume estimates rather than those suggested by clinical impression This was of obvious benefit to our patients The patients who illustrate this best are those suffering from very large wounds and much blood loss, who, as a result of blood volume estimations, were given very large transfusions that would otherwise have been thought far beyond their requirements Why such very large transfusions are required is as yet not clear, but there was no doubt of the great clinical improvement these patients showed by comparison with similar cases given less In no patient transfused with volumes of blood and plasma calculated from the results of blood volume estimation was any evidence of overtransfusion seen

B Transfused Fluids

The protein-containing fluids used for transfusion were fresh blood, stored blood, reconstituted dried serum and dried plasma Fresh blood was drawn at the Forward Surgical Centre into isotonic citrate solution and usually transfused within 24 hr , but occasionally only within 48 hr , of withdrawal Stored blood was prepared at the Base Transfusion Depot and a pint bottle contained approximately 450 ml of blood, 100 ml of 3 per cent trisodium citrate solution, and enough glucose solution to give a final concentration of about 500 mg per 100 ml , it was always of Group O By our analyses the average composition of a bottle of blood, fresh or stored, was about 200 ml of red cells and about 14 g of plasma protein The dried pooled serum and the dried pooled plasma were reconstituted with distilled water or glucose saline (0 3 per cent NaCl, 5 per cent glucose) to volumes of 500 ml (serum) and 400–540 ml. (plasma) An average bottle of plasma contained about 18 g protein in a concentration of 3 3–4 5 g per 100 ml

The average level of plasma protein in injured soldiers estimated to have lost 30 per cent or more of their blood was about 6 g per 100 ml Supposing

that the protein transfused remains in the circulation, then transfusion of the protein contained in one bottle of plasma will increase the blood volume by about 300 ml. (about 5 per cent of the blood volume of an average soldier), and of that contained in one bottle of serum by 500 ml. (or about 9 per cent of the blood volume of an average soldier), while one bottle of fresh blood will increase it by about 450 ml. (about 8 per cent of the normal blood volume). The increase in blood volume caused by a bottle of stored blood will depend on the conditions of storage; a large proportion of the total red cells of badly stored blood may be removed in a short period after transfusion (Gibson, Peacock, *et al.*, 1947), whereas the red cells of transfused blood that has been well stored may have as long a life as those of fresh blood (Mollison and Young, 1942; Gibson, Evans, *et al.*, 1947). It has been shown that the nonviable red cells of stored blood are removed chiefly in the first few hours after transfusion and that the removal is complete within 24 or at most 48 hr. (Gibson, Peacock, *et al.*, 1947). A bottle of well stored blood containing 200 ml. red cells and 250 ml. plasma will, allowing for a 10 per cent loss of red cells in the first few hours after transfusion, increase the blood volume by 430 ml., or about 8 per cent of the total blood volume of man. With badly stored blood as much as 50 per cent of the total red cells may be removed within a few hours, and in such a case the increase in blood volume will only be 350 ml., or about 6 per cent of the blood volume of an average soldier.

Through lack of facilities it was not possible to measure the length of life in injured patients of transfused stored red cells. The freshest blood available was transfused to the patients we studied; it had usually been stored for less than ten days, often for less than five. Such blood, reasonably well stored in trisodium citrate glucose solutions, should only lose at the most 20 per cent of its red cells in the first few hours after transfusion, and thereafter the red cells would be expected to decline by not more than a few per cent per day. At times, however, it is probable that the blood was not well stored. Many estimations of plasma haemoglobin and bilirubin were made, though not with the specific object of testing the storage of the blood. A raised plasma haemoglobin would have suggested rapid breakdown of transfused red cells, but levels above 10 mg. per 100 ml. were not often encountered. It is possible, however, that transfused red cells are removed from the circulation and broken down without liberating haemoglobin into the circulation. It is difficult to interpret plasma bilirubin levels since these depend not only on the formation of bilirubin but on the excretory activity of the liver.

C. Volume of Transfusion Required by Patients Suffering Very Large Injuries

In the foregoing pages it has been shown that patients suffering from very large injuries require *very large transfusions* and respond well to them. Since the volume of the fluids transfused may seem unduly large, and the fate of the red cells and protein transfused requires more analysis, some further details are noted here.

In Table 47 are shown details of three soldiers who suffered from very large wounds, from which rough balance observations may be made There is most information about *I* 109 and *I* 110 In column (3) are shown the numbers of bottles of blood, serum and plasma and the total volume of fluid transfused to each case in the first 24 hr after injury In column (4) rough estimates of the patient's red cell volumes and plasma protein before transfusion started are shown on the assumption that at this time 50–60 per cent of their blood had been lost by bleeding In column (5) are shown the total grammes of plasma protein and the total volumes of red cells transfused and assumed to be viable, the latter calculated as 90 per cent of the estimated total volume of red cells transfused, allowing for a 10 per cent removal of the stored red cells during the first 24 hr In column (6), for subjects *I* 109 and *I* 110, are shown dye haematocrit estimates of total red cells and total plasma protein In Case *I* 108 no dye estimates were made and a guess is therefore shown In column (7) are shown the results of rough balances derived from the differences between the values of column (6) and the summed values of columns (4) and (5) It can be seen that in each case, in spite of very great transfusion, there is a considerable negative balance amounting to about half the subject's initial total red cells and plasma protein Excluding *I* 108, in whom the balance has been guessed, the missing red cells and plasma protein in subjects *I* 109 and *I* 110 are in proportions which suggest that they might mainly represent loss of whole blood The observations in columns (6) and (9) also show that, in spite of the large transfusions, all three patients were suffering from a lack rather than an excess of haemoglobin and plasma protein All three pursued a clinical course much smoother than others suffering from very large wounds but given less transfusion, which strongly suggests that very large transfusions are the correct treatment for the majority of such cases All three, moreover, started to pass urine freely within 24 hr of injury, which is uncommon in those with similar wounds who have been transfused less

The question arises in what ways such large volumes of red cells and protein were lost The possible causes of such loss in the first 24 hr after injury are summarized below

Loss of whole blood	External haemorrhage before, during or after operation
	Haemorrhage into damaged tissues
Loss of red cells only	
(*a*) Patient's	Removal by reaction with transfused agglutinins
(*b*) Transfused	Removal because imperfectly stored
(*c*) Both	Removal by possible haemolytic systems from damaged tissues
	Apparent removal by trapping in the circulation
Loss of plasma proteins only	Leakage into damaged or other tissues
	Trapping in part of the circulation
	Metabolism of transfused protein
	Removal as a result of transfusion of fluid

TABLE 47

Red cells and protein lost from the circulation by subjects with very large wounds during the first day after injury

Patient	(1) Injuries	(2) Blood group	(3) Transfusion in 1st 24 hr					Balance calculations				(8)		(9) 24 hr after injury		(10) Comments
			Blood (bottles)	Plasma (bottles)	Serum (bottles)	Fluid (ml)		(4) Before transfusion	(5) Transfused in 1st 24 hr	(6) 24 hr after injury (max estimate)	(7) Negative balance (6)—((4)+(5))	Max observed plasma Hb (mg per 100 ml)	Max observed bilirubin (mg per 100 ml)	Hb (g per 100 ml)	Plasma protein (g per 100 ml)	
I 110	See pages 33, 73 and 86	A	11	—	3	7500	Red cells (ml) Plasma protein (g)	1000 100	2000 240	1900 225	1100 115 ≡ 1900 ml plasma	20	1·6	10	5·7	Lost much blood before and during operation, and some after, by oozing into dressing and plasters
I 109	See page 79	A	6	6	—	5600	Red cells (ml) Plasma protein (g)	1000 100	1100 190	1050 185	1050 105 ≡ 1700 ml plasma	2	3·6	8	6·2	External blood loss before and during operation, and some into dressings and plasters after operation
I 108	See pages 47, 74 and 83	O	13	—	3	8200	Red cells (ml) Plasma protein (g)	1000 100	2300 270	?2000 ?200	?1300 ?170	—	—	9·5	5·5	Probably much external haemorrhage

In each case it is assumed that in Column (4) each subject has lost 50–60 per cent of his initial protein and red cells before admission These amounts must therefore be added to the figures shown in Column (7) to get estimates of the total red cells and protein lost in the first 24 hr after injury

In Column (5) the volume of red cells is estimated as 90 per cent of the volume transfused, a 10 per cent allowance being made for removal of non-viable red cells

In Column (6) the maximum estimates are derived from dye estimates of blood volume made within a few hours of the time shown, no blood volume estimates were made for *I* 108, for whom these values have been guessed

It is thought that the chief loss of red cells and plasma after admission to the Surgical Centre was from blood lost externally or into the tissues, attempts to measure the blood lost externally by *I* 109 and *I* 110 failed But clinical impression was that this alone could not account for the observed negative balances The blood lost into the tissues could not be measured, but much of it was probably lost before admission and therefore does not come into these balances It is probable that a fair amount of blood would be lost after operation, since the wounds were laid open widely, skin flaps of amputation stumps were loosely sutured, and both were then covered in plaster, the plasters of *I* 109 and *I* 110 became discoloured after operation by bloody effusions

Other causes which may have played some part in the negative balances include the removal of red cells from blood which has been badly stored An allowance of 10 per cent for removal of red cells has been made in these cases, which is probably justifiable, since the blood given to *I* 108 had been stored for at most four days, that given to *I* 110, except two bottles five days old, was three days old, and that given to case *I* 109 was seven days old

Observations on the plasma haemoglobin of *I* 109 and *I* 110 suggest that haemolysis of the transfused red cells did not occur to any great extent These patients were Group A but were transfused large volumes of Group O blood The anti-A titre of this blood could not be measured, but it is known that transfusions of plasma with a high anti-A titre to subjects with group A red cells may result in removal of the subject's own red cells (Ebert and Emerson, 1946, Gibson, Aub, *et al*, 1947) However, the case of *I* 108, blood Group O, who despite being transfused greater quantities of blood and serum than the other two showed no evidence of overtransfusion, and probably had a negative balance of the order shown, suggests that this did not play a major part

As noted earlier, marked vasoconstriction may cause dye methods to underestimate the blood volume At the time the dye estimations were made in *I* 109 and *I* 110 these subjects had received much transfusion and their slight degree of vasoconstriction was not thought to be playing a significant part in the negative balances observed Later observations gave no evidence of a release of red cells trapped in the circulation

There are two other possible explanations of protein loss It is held that transfusion of large volumes of fluid may result in removal of protein from the circulation Plasma protein can be metabolized to satisfy the body's nitrogen requirements (Elman, 1944) It is thus possible that transfused protein was carried into the tissue fluids with transfused fluids and that some of it was metabolized

These observations may be summarized thus Patients with very large wounds usually require very large transfusions, much more than even a bold transfusion officer is inclined to give till he has learnt for himself It is probable that the chief reasons why these very large transfusions are required are (*a*) to replace the large quantities of blood lost externally and into the tissues, and (*b*) because of the imperfections of the fluids transfused Much further analysis is, however, required

D. Haematological Changes

In this section observations on the changes in haemoglobin and plasma protein concentrations, the haematocrit, the plasma volume and the total red cell volume are summarized. The relationship between the changes and the circulatory state has been dealt with in Parts I and II and is not considered here. The methods of estimating haemoglobin, haematocrit, plasma protein and plasma and red cell volume were those described in Section A.

LIMB INJURIES

In Part I it has been shown that patients suffering from limb injuries, seen soon after injury, have often lost very large quantities of blood, the amount lost being roughly proportional to the volume of tissue damaged. In such cases the concentrations of haemoglobin and plasma protein and the volume of plasma and red cells must depend on (*a*) the volume of blood lost and (*b*) the quantities of red cells, fluid and plasma protein added to the blood after haemorrhage, whether by the patient's tissues or by transfusion.

The responses of man's circulation to haemorrhage are best studied after measured venesections, for by this means possible influences of damaged tissue are avoided. Few experimental observations, however, have been recorded of the effects on human blood volume, haemoglobin and plasma protein concentrations of venesections of the order of 20 per cent of the blood volume, and none of venesections of 30 per cent or more. According to Ebert and Stead (1941) fit men respond to venesections of 15–20 per cent of their blood volume by diluting the remaining blood, first, and rapidly, with fluid poor in protein, but after a few hours with new plasma containing the plasma proteins in the same proportion as the original plasma, but a little more dilute. It is probable that no new red cells are added to the circulation in the first three or four days after such haemorrhage, but by this time the blood volume has been raised to close to its original level by the addition of new plasma. There is no evidence in man of depots which can liberate significant quantities of red cells into the circulation in response to haemorrhage (for references see Reeve, 1948).

If injured patients respond to various degrees of haemorrhage in the same general way as venesected subjects from whom relatively small amounts of blood have been withdrawn, they would be expected to show an initial rapid dilution of haemoglobin and plasma protein, followed by a further slower dilution of haemoglobin with the plasma protein concentration remaining about constant. During the first few days after injury the total red cell volume would be smaller by the amount of red cells lost in haemorrhage, whereas the plasma volume, at first decreased by the amount lost in haemorrhage, would increase progressively until by the third or fourth day the blood volume was restored to near its original level. The greater the haemorrhage, the greater the fall of haemoglobin to be expected.

Transfusions of plasma and blood would be expected to modify the above course of events, plasma transfusion resulting in a more rapid dilution of the haemoglobin and a more rapid increase in blood volume, blood transfusion,

because of the transfused red cells, in a more rapid increase in blood volume but less dilution of the haemoglobin

The course of the actual blood changes in injured patients is now examined to see how closely it reproduces the above picture

Early Blood Changes and their Interpretation before Transfusion

Haemoglobin

Fig 8A shows the haemoglobin concentrations of the first samples of blood drawn from a series of untransfused patients with limb injuries suffering from different amounts of tissue damage and blood loss The figure is divided into three vertical sections, the section on the left containing those patients estimated to have lost 20 per cent or less of their blood, the middle section those estimated to have lost 21–40 per cent, and the right hand section those estimated to have lost more than 40 per cent Blood loss was estimated from blood volume estimations made as soon as possible after injury and before, or after a minimum of, transfusion (as described in Section A) In each compartment the initial haemoglobin concentration is plotted against the time of sampling after injury The amount of tissue damage is also shown During the first 12 hr after injury, it will be seen that in each section there is a considerable scatter of values, but a comparison of the three sections shows that the mean haemoglobin of those estimated to have lost 20 per cent or less of their blood is about 95 per cent, that of those estimated to have lost 21–40 per cent about 86 per cent, and that of those estimated to have lost more than 40 per cent about 74 per cent The great majority of these patients were fit, front-line troops who, it may be presumed, had before wounding a haemoglobin concentration near 100 per cent (16 g haemoglobin per 100 ml) It is clear, therefore, that in general the greater the estimated initial haemorrhage the lower the initial haemoglobin

From these data, approximate calculations may be made of the average amounts of fluid added to the blood after haemorrhage and before transfusion. If the initial haemoglobin value is taken as 100 per cent and the average haemorrhage of the centre section as 30 per cent of the initial blood volume, then after a reduction of the blood volume to 70 per cent these patients on the average added ($70 \times 100/86 - 70$), or about 11, per cent of their initial blood volume from their tissue fluids Using the same method and taking the mean initial haemorrhage of the group in the right hand section as 50 per cent of the blood volume, then this group on the average added ($50 \times 100/74 - 50$), or about 18, per cent of their initial blood volume Eleven per cent of an initial blood volume of 5,500 ml is equivalent to 605 ml, 18 per cent to 990 ml, so it would seem that during the first few hours after considerable haemorrhage a man may add 500–1,000 ml of fluid to his blood In the present state of knowledge of distribution of red cells and plasma in the circulation these estimates cannot be regarded as precise, but they are probably not greatly in error

Plasma Protein

In Fig 8B are plotted the initial plasma protein concentrations of the samples drawn before transfusion from the same series of patients with limb

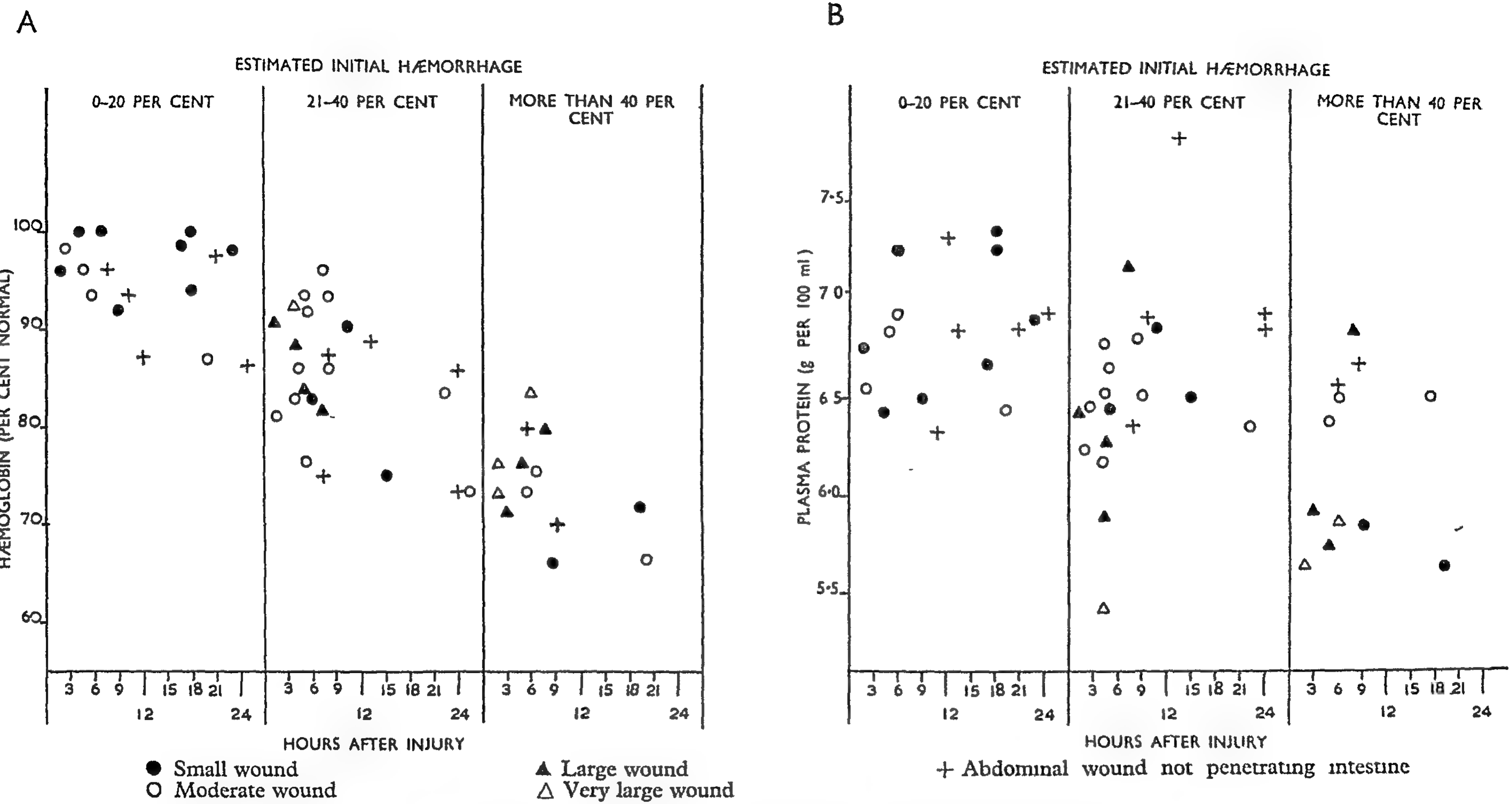


Fig 8 (A) Initial haemoglobin and (B) plasma protein concentrations in battle casualties with limb injuries or abdominal wounds not penetrating the intestine

N.B 1 Plasma protein concentrations were not obtained for two cases shown in 8A
2. One hundred per cent haemoglobin is taken as 16 g per 100 ml.

injuries The patients are divided into the same three groups, and in each group the plasma protein concentration of the sample is plotted against the time between injury and sampling In each group, again, there is a considerable scatter of values, but the mean value falls as the estimated haemorrhage increases Thus the mean protein value of those estimated to have lost less than 20 per cent of their blood is 6 8 g per 100 ml, of those estimated to have lost 21–40 per cent, 6 4 g per 100 ml, and of those estimated to have lost more than 40 per cent, 6 0 g per 100 ml

The average amount of fluid entering the plasma to dilute the proteins may be calculated If the average initial plasma protein is 7 0 g per 100 ml, those estimated to have lost 21–40 per cent of their blood diluted their plasma by $(7\ 0 \times 100/6\ 4 - 100)$, or 9, per cent thus an initial plasma volume of 3,000 ml will be reduced to 2,100 ml by a 30 per cent haemorrhage and diluted to about 2,300 ml by the addition of sufficient fluid to reduce the protein concentration from 7 0 to 6 4 g per 100 ml Similarly a haemorrhage of 50 per cent will reduce the plasma volume to 1,500 ml, and the volume will be increased to about 1,750 ml by the addition of sufficient fluid to reduce the protein concentration from 7 0 to 6 0 g per 100 ml

Thus in the first 12 hr after considerable haemorrhage a man can add on the average only 200–250 ml of protein-free fluid, and a haemorrhage of the order of 50 per cent results in little more protein-free fluid being added to the plasma than does a haemorrhage of the order of 30 per cent

The differences between these amounts and those derived above from the haemoglobin dilutions give a rough estimate of the amounts of new protein-containing plasma added to the circulation after haemorrhage Such calculations indicate that a man unaided by transfusion can add 400–750 ml of new plasma in the first 12 hr after much haemorrhage

It will be noted that the three patients shown in Fig 8B as suffering from very large injuries all had initial protein concentrations of 5 8 g per 100 ml or less, though one of them was estimated to have lost initially only about 30 per cent of his blood In such cases some protein leak into damaged tissues cannot be excluded Such a leak would cause this method to overestimate the amount of protein-free fluid added

Changes in Average Red Cell Volume

Haematocrit values will parallel the haemoglobin concentration unless swelling or shrinkage of the red cells occurs The observations of Dyson, Plaut and Vaughan (1944) suggest that swelling of the red cells may occur after venesections of as little as 540 ml of blood

The mean corpuscular haemoglobin concentration may be used as an index of average red cell volume, it is defined as the quantity of haemoglobin in grammes contained in 100 ml of packed red cells and is derived from the formula

$$\frac{\text{Grammes haemoglobin per 100 ml. blood}}{\text{Haematocrit per cent}} \times 100$$

In a series of samples drawn from the same patient a decrease in this concentration indicates swelling of the red cells and *vice versa* Estimates of both haemoglobin concentration and haematocrit are required to determine the mean corpuscular haemoglobin concentration, so the values obtained will show variations due to the combined

errors of the two estimates To determine the amount of this variation a statistical analysis has been made of 83 estimates of mean corpuscular haemoglobin concentration in 83 samples of blood drawn from 11 patients, all previously fit troops suffering from minor complaints of short duration. Five to ten samples of blood were drawn from each patient over periods of 1–3 hr. for the purpose of blood volume observations. Assuming that during this period in each patient the mean corpuscular haemoglobin concentration remained constant, the errors of estimation of this quantity may be determined from the observed variations in the estimates on the samples drawn from each patient. The standard deviation is 0 63. The mean estimate of the mean corpuscular haemoglobin concentration of these 11 patients was 33 0 with a range of 31 9 to 33 7; i.e. the range is within the errors of estimation.

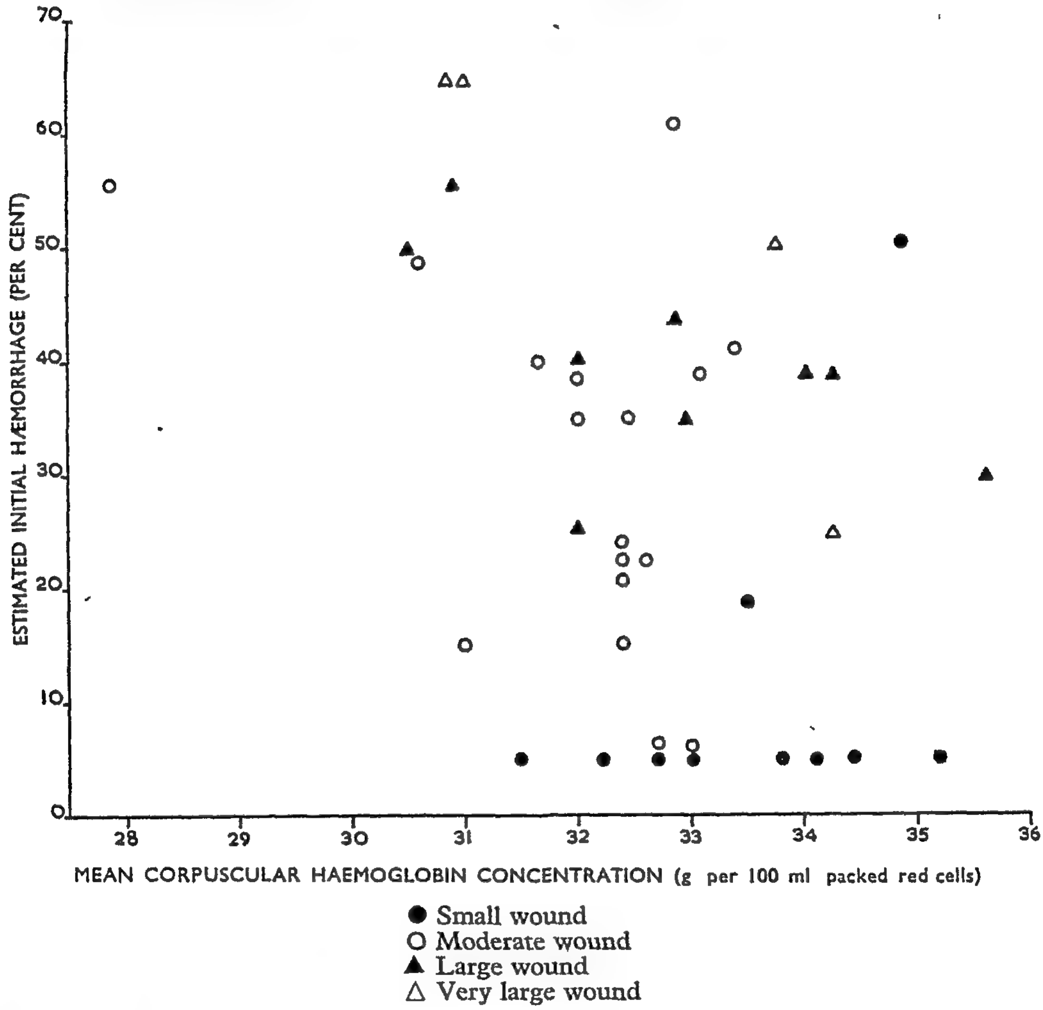


FIG. 9. Changes in average red cell volume after injury

Fig. 9 is a scatter diagram of the early post-injury mean corpuscular haemoglobin concentrations of 40 untransfused patients with limb injuries, plotted against estimated initial haemorrhage. The majority of the values fall between 31 0 and 35 0, irrespective of the size of wound and the amount of haemorrhage. The mean value for the 20 patients estimated to have lost 30 per cent or less of their blood is 33 05 with a standard deviation of 1.18; that of the 20 estimated to have lost more than 30 per cent is 32 16 with a standard deviation of 1 6. The significance of the difference between the two means may be tested with Fisher's (1946) t test. Application of the test shows that t is 2 01

for 38 degrees of freedom, which gives a value of P close to 0 05 Thus this difference between the means is barely significant i e patients suffering great haemorrhage do not consistently show more swollen red cells than those suffering smaller amounts of haemorrhage

A rough estimate of the maximum amount of red cell swelling can be made Seven cases in Fig 9 show mean corpuscular haemoglobin concentrations of 31 or less, six of these were estimated at the time to have lost 50 per cent or more of their blood, and their mean corpuscular haemoglobin concentration was 30 0 Assuming that the average mean corpuscular haemoglobin concentration was 33 0 (to support this assumption it may be noted that in the subsequent samples drawn from these six patients over the next three days, after much transfusion, the mean value was 32 8) and that after haemorrhage 1,200 ml of red cells remained, then these red cells swelled by (1,200 × 33 0/30 — 1,200) ml, that is by 120 ml or 10 per cent of their initial volume This change in volume is not great

Blood Volume

Much of the evidence that has been presented in the foregoing pages to show that the initial blood volumes after great haemorrhage are very considerably reduced will be found summarized in Table 6, p 16 The blood volumes measured after haemorrhage should approximate to the red cells and plasma remaining after haemorrhage plus the fluid added by dilution Thus after a 30 per cent haemorrhage the blood volume should approximate to the 70 per cent of the blood remaining plus about 11 per cent of added diluent fluid, or to about 81 per cent of normal, and examination of Table 6 shows this to be approximately true After a 50 per cent haemorrhage the blood volume should approximate to the 50 per cent of blood remaining plus about 18 per cent of added diluting fluid, or to about 68 per cent of the normal blood volume, and examination of the table again shows that this is approximately correct Individual variations in the rate and extent of dilution will cause variations in these figures

Discussion

Other workers' findings There are few other published descriptions of battle casualties suffering from injuries to the limbs from which data such as those in Fig 8A and B can be derived We have examined in similar fashion the data in the reports of Keith (1919), Emerson and Ebert (1945) and Chute, Cleghorn and Lathe (1945) The majority of the patients observed by Chute *et al* and Emerson and Ebert had been transfused before they were seen These two groups of authors report only haematocrit values, but haemoglobin values can be derived on the assumption that a haematocrit of 47 per cent was equivalent to a haemoglobin concentration of 100 per cent * There are 9 patients who from blood volume estimations may be considered to have lost initially 21–40 per cent of their blood, haemoglobin estimations made

*The usually accepted mean value for mean cellular haemoglobin concentration is 34 0 (Wintrobe, 1946) and this value is used here when dealing with other workers results and in some of the figures Our mean value was 33·0

3–14 hr. after injury averaged about 88 per cent with a range of 81–95 per cent. There are 13 patients who may be considered to have lost more than 40 per cent of their blood; haemoglobin estimations made 2–14 hr. after injury averaged about 78 per cent with a range of 61–91 per cent. Thus these observations agree with ours. The observations on plasma protein concentrations are too few to warrant analysis.

Practical rules. It has often been stated that haemoglobin estimations made before transfusion in the first few hours after wounding are of no use in estimating the amount of blood lost. This is not true. From examination of the data shown in Fig. 8A it may be stated that, between 3 hr. and 12 hr. after injury: (1) a haemoglobin concentration above 90 per cent (14·4 g. per 100 ml.) indicates a blood loss of less than 40 per cent; (2) a haemoglobin concentration below 75 per cent (12 g. per 100 ml.) indicates haemorrhage of more than 40 per cent; (3) a haemoglobin concentration of 75–85 per cent (12–13·6 g. per 100 ml.) indicates a blood loss of 20 per cent or over. These rules can only be applied to a population of fit troops and refer to estimates of haemoglobin by precise methods on venous samples drawn without stasis. They might not apply in very hot or very cold climates, and certainly do not apply to less fit civilian casualties.

Rate of dilution It is possible that after haemorrhage associated with much damaged tissue the course of dilution might be modified. In Figs 8A and B the early course of dilution in small and moderate wounds can be compared with the early course in large and very large wounds. Such comparison reveals no evidence of a difference in the rates of dilution between these two groups, suggesting that the presence of much damaged tissue does not alter the early course of dilution.

Effects of Transfusion on Blood Dilution

Plasma Transfusion

The plasma used in transfusing these cases for the most part had a lower protein content than the patient's plasma. Thus one bottle of plasma contained about 18 g. plasma protein dissolved in 400 and sometimes 540 ml. of fluid (protein content 3·3–4·5 g. per 100 ml.) and one bottle of blood contained about 14 g. of protein dissolved in about 340 ml. of fluid (protein content about 4 0 g. per 100 ml.). Only the serum was usually administered in a concentration (about 6 0 g. per 100 ml.) close to that of the patient's plasma. It is well known that crystalloid solutions given intravenously rapidly leave the circulations of normal and injured men. In our patients we rarely found plasma protein concentration changed by more than $\pm$ 0·5 g. protein per 100 ml. as a result of transfusion, suggesting that the major part of the transfused diluent left the circulation. Table 45 (p. 247), taken from the results of Emerson and Ebert (1945), provides further evidence of this. It can be seen that, in the instances of limb injury quoted there, large quantities of transfused diluent left the circulation and in four out of the six examples the change in plasma protein concentration after transfusion was $\pm$ 0 3 g. per 100 ml. or less. With a final plasma volume of 3,500 ml. a fall in protein concentration from 6·5 to 6 0 g. per 100 ml. as a result of transfusion indicates that less than 300 ml. of the transfused diluent was retained in the circulation.

Case I 53 illustrates the effects of large plasma transfusions given to patients who had bled much

Case I 53, estimated to have lost 50–60 per cent of his blood, at 6½ hr after injury and before transfusion had a haemoglobin of 76 per cent and a plasma protein of 6 5 g per 100 ml Eight hours later, after having received 150 g protein in 2,500 ml fluid, his haemoglobin was 42 per cent and his plasma protein 6 8 g per 100 ml

In Fig 14 (p 283) data taken from Emerson and Ebert (1945) and Chute *et al* (1945) and some of our own data also show the effects of transfusions of plasma, given soon after injury, on the haemoglobin and plasma protein concentrations of patients with limb injuries who were estimated to have lost more than 40 per cent of their blood It is clear that transfusions of plasma, given to patients who have bled much, cause profound falls in the haemoglobin level

Blood Transfusion

One bottle of stored or fresh blood contained about 440 ml of whole blood drawn from fit donors and about 100 ml of anticoagulant diluent From the observations already made it would be expected that most of the transfused diluent would leave the circulation rapidly, leaving behind plasma, usually of a protein content of 6 0 g per 100 ml or more, and the red cells The haemoglobin concentration of the transfused blood remaining in the circulation would then be expected to be about 80–90 per cent Large transfusions of this blood to patients who had bled much would therefore be expected, unless a proportion of the red cells was rapidly removed from the circulation, to bring the haemoglobin levels towards about 80 per cent This rough generalization appears to be true of the few of our cases estimated to have lost 40–50 per cent of their blood who were transfused four or five bottles of blood and little or no plasma during the first 36 hr of their course However, to conserve supplies of blood, most of our cases were transfused with both blood and plasma As can be seen in Fig 10 B, C and D, in the great majority of cases by 48 hr after injury this reduced the haemoglobin to levels of 60–70 per cent, and in some cases lower

We made no blood volume measurements specifically to estimate the quantity of transfused red cells and plasma protein remaining in the circulation over short periods, but the observations of Emerson and Ebert quoted in Table 45 (p 247) indicate that in favourable circumstances a large proportion of the transfused red cells and plasma protein remained in the circulation

The Course of Blood Dilution and its Interpretation

Later Blood Volume Levels

Table 48 shows the results of plasma and red cell volume estimations made 56–104 hr after injury on 15 patients with limb injuries The estimated haemorrhage at the time of injury, the total amounts of blood and plasma transfused, and the percentage of the predicted normal plasma, red cell and total blood volumes are also shown It will be noted that, as shown by the

TABLE 48

Blood volume estimates three to four days after injury

Patient	Estimated initial blood loss (percentage predicted normal blood volume)	Time after injury (hr.)	Transfusion given before estimation (bottles)			Plasma volume		Red cell volume		Blood volume (percentage predicted normal)
			Blood*	Plasma†	Serum‡	ml.	Percentage predicted normal volume	ml	Percentage predicted normal volume	
I. 88	21–30 per cent	75	—	—	—	3520	134	1260	54	97
I. 40	,,	56	—	—	—	2540	118	1170	61	92
I. 60	,,	80	—	6	—	3260	95	1790	58	78
I. 22	31–40 per cent	93	1	1	—	3200	116	1170	48	84
I. 70	,,	94	1½	—	1	3780	137	1090	45	94
I. 57	,,	63	2	2	—	2560	105	1060	49	80
I. 68	,,	95	3	1	—	2840	121	1480	71	99
I. 46	,,	71	1	2	—	3250	115	1280	51	85
I. 58	41–50 per cent	104	5	—	—	3140	111	1760	70	93
I. 84	,,	94	2	3	—	3330	115	1030	40	80
I. 23	,,	64	3	—	—	3320	113	1630	62	90
I. 85	Above 50 per cent	93	5	5	—	3510	117	1270	48	86
I. 109	,,	89	9	6	—	3470	120	1700	66	94
I. 110	,,	71	11	—	3	4050	134	1470	54	97
I. 53	,,	80	—	10	—	3440	114	720	27	73

* 1 bottle of blood contained 540 ml. blood and preservative solution, about 200 ml. red cells and 14 g. protein
† 1 bottle of plasma contained about 18 g. protein in 400–540 ml. of fluid
‡ 1 bottle of serum contained about 30 g. protein in 500 ml. fluid.

serial numbers, the wounds range from moderate to very large, the estimated initial haemorrhage from 21 per cent to over 50 per cent, and the transfusion from none to 11 bottles of blood and 3 of serum In none of these patients did the blood volume reach its predicted normal value, though in several it was close to it In 7 it was below 90 per cent of the predicted normal and in 4 it was 80 per cent or less (In all cases who lost a limb or part of a limb through injury or surgery the predicted normal blood volume was reduced to allow for the resulting shrinkage of the vasculature) Thus it can be seen that in the first three or four days after the injury none of these injured patients "over-diluted", that is to say none raised their blood volume above its pre-injury level, and a number failed to raise it to within 90 per cent of that level

Haemoglobin Levels

Fig 10 shows the course of the haemoglobin changes during the first few days after injury of a series of soldiers suffering from limb injuries The cases are divided into four groups on the basis of the estimated initial haemorrhage, in Section A it was 20–30 per cent of their blood, in Section B 31–40 per cent, in Section C 41–50 per cent and in Section D more than 50 per cent All but two received transfusions of plasma, blood or both, the numbers of bottles of blood each case received are indicated by the circled figures placed at the end of each case's graph It will be seen that in Fig 10A, B and C the haemoglobin levels at first fell rapidly, but by 70 hr after injury in the majority the rate of fall was much reduced or stopped This is also on the whole true of Fig 10D though, because of the considerable whole blood transfusions, the picture is less clear cut

If the initial haemorrhage is solely or mainly responsible for the loss of red cells and the blood volume is restored to near normal by the third or fourth day after injury, then, unless blood has been transfused, the haemoglobin level after an initial 30 per cent haemorrhage should be about 70 per cent, after a 40 per cent haemorrhage about 60 per cent, and so on If the blood volume has not been restored to normal then the haemoglobin levels should be higher than this—for instance after a 40 per cent haemorrhage with blood volume restoration to 80 per cent normal the haemoglobin level would be about 75 and not about 60 per cent The addition of red cells by transfusion will also affect these levels Making the conservative assumption that 150 ml of the red cells of each bottle of blood transfused remained in the circulation for the next 3–5 days, and taking a high average value of 2,500 ml of red cells as the normal volume of total red cells in these cases, then if the blood volume is restored to near its normal level the addition of 150 ml of red cells should raise the haemoglobin level by 6 per cent On this basis it would be expected that if after a 50 per cent haemorrhage a subject is transfused with four bottles of blood and the blood volume is restored to near normal levels the resulting haemoglobin concentration should be (50 + 24) or 74 per cent If the blood volume is not restored to normal levels the haemoglobin level should be still higher

In Fig 10A, by 70–100 hr after injury the haemoglobin level had fallen on the average to about 60 per cent, though three of the cases received blood

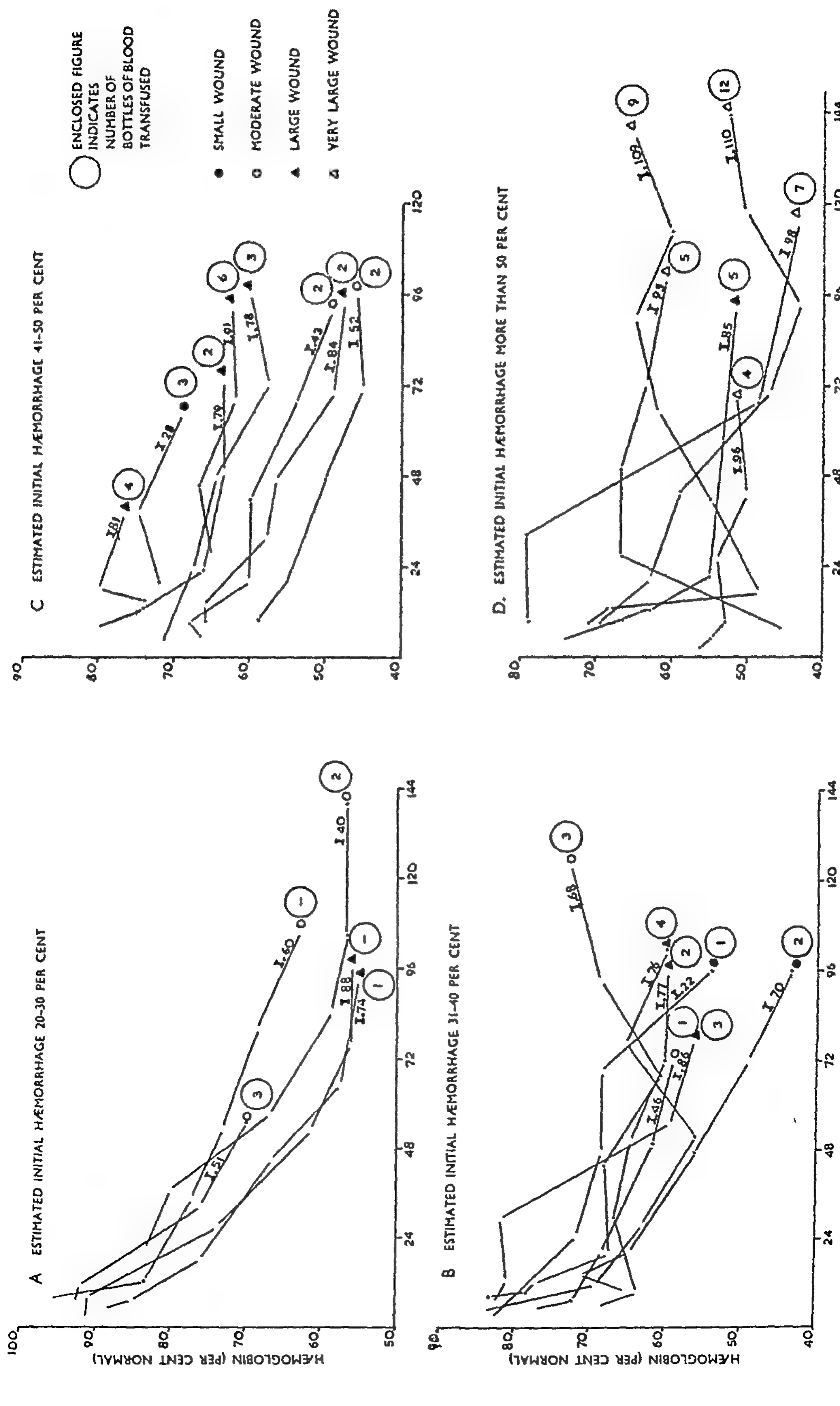


FIG. 10 Haemoglobin changes in patients with limb injuries

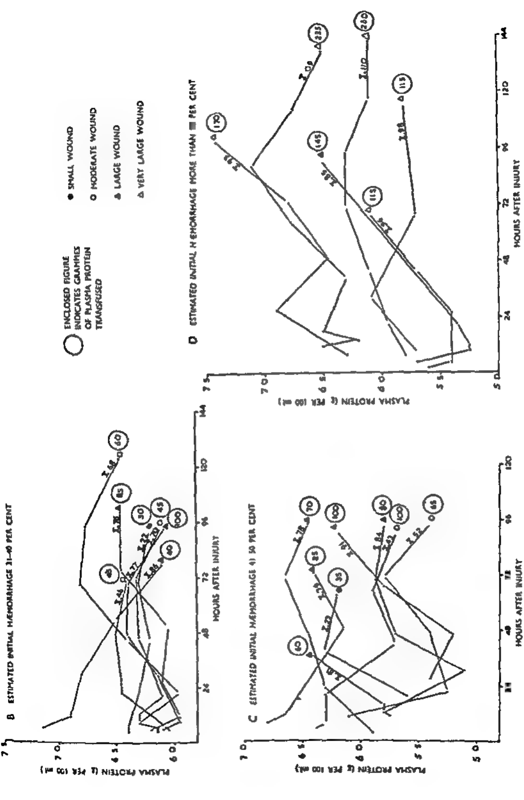


FIG 11 Plasma protein changes in patients with limb injuries

transfusions. The maximum fall to be expected from the estimated initial haemorrhage, neglecting the effects of the transfused red cells in three of the cases, would be to 70 per cent haemoglobin. Also in Fig. 10B it can be seen that the mean haemoglobin level at 70–100 hr. after injury was about 60 per cent, though every case had received transfusions of from one to four bottles of blood. The maximum expected fall of haemoglobin, taking an average of two bottles of transfused blood, would be to about 72 per cent. In Fig. 10C the average haemoglobin level at 70–100 hr. after injury was about 55 per cent, though these subjects had been transfused with two to six bottles of blood. It will be observed that those transfused the greater quantities of blood had the higher haemoglobin levels. Taking an average of three bottles of blood transfused, the maximum fall in haemoglobin should be to 68 per cent. In Fig. 10D the average haemoglobin level at 70–100 hr. after injury is again about 55 per cent and transfusion ranged from four to twelve bottles of blood. If each case had only received five bottles of blood and each had lost 60 per cent of his blood initially, then the lowest expected haemoglobin level at this time would be 70 per cent. This evidence strongly suggests that these patients lost more red cells than could be accounted for by their estimated initial haemorrhages.

Plasma Protein Levels

In Fig. 11B, C and D are shown plasma protein concentrations of the same patients as dealt with in Fig. 10B, C and D: the data corresponding to Fig. 10A have been omitted. The plasma protein concentrations were determined on the same samples of blood as the haemoglobin concentrations, and are plotted against the time of sampling after injury. The amount of tissue damaged is again shown, and in the circle at the end of the graph of each case the total quantity of plasma protein tranfused is indicated in grammes. It will be seen that the protein concentrations of the majority of cases did not fall much below 6 g. per 100 ml. and that there was a much smaller percentage dilution than in the corresponding haemoglobin values.

Five cases in Fig. 11C and D show plasma protein levels in the region of 5·5 g. per 100 ml., and there were three other cases, not shown in the figures, with similar levels; seven out of this total of nine were suffering from large or very large injuries, the other two from moderate injuries. The reasons for these rather lower values are not clear and may be multiple, one possibility being protein leakage into damaged tissues. It should be noted that they are not an invariable accompaniment of large injury. Fig. 11D shows that patients with very large wounds who have been given large quantities of plasma may have plasma protein levels well above 6·0 g. per 100 ml.

Balance Observations

It has been seen that the course of haemoglobin dilution strongly suggests greater losses of red cells than those estimated to have occurred up to the time of admission to hospital. Estimations of blood lost at operation and repeated estimates of blood volume throw further light on this loss. In Table 49 are shown details of a number of patients with limb injuries at various times in their course. For each patient the size of wound and the estimated initial

haemorrhage are shown, with the total amount of red cells and plasma protein transfused before the first blood volume estimation and between this and the second, together with the estimated blood loss at operation in ml of red cells and g of plasma protein A 25 per cent loss after transfusion has been allowed for by taking the content of one bottle of blood as 150 ml red cells One bottle of plasma was taken to contain 18 g protein, one bottle of blood 14 g, and one bottle of serum 30 g If the two estimates of red cell volume and plasma protein by the blood volume method are correct, if the estimates of loss at operation are correct, and if the red cells and plasma protein transfused remained in the circulation, then the second blood volume estimate of red cells and plasma protein should be equivalent to the first plus the total transfused red cells and plasma protein minus the red cells and plasma protein lost at operation The column marked "balance" shows the results of such calculations, the prefix "−" shows loss of red cells or plasma protein, the prefix "+" a gain

The table is divided into three sections Section A contains repeated estimates separated by intervals of 3½–6 hr during which operation took place, so the balance shows changes taking place immediately before operation, during it and immediately afterwards In *Case I* 104, with very large wounds, the balance shows a loss of 80 ml of red cells and 9 g of protein, which is well within the errors of the methods In the other four patients the losses of red cells on balance vary from 200 to 420 ml and the losses of plasma protein from 8 to 35 g, suggesting that there was a real and considerable loss of red cells, and in *Cases I* 76 and *I* 86 a loss of plasma protein, not to be accounted for by operation blood loss

Section B contains five repeated estimates separated by intervals of 14–20 hr The first blood volume estimate in each case was made shortly before operation and the second a number of hours after, so that the balances reflect losses or gains not only immediately before and during operation, but also during the first 12 hr or so after operation It will be observed that *Case I* 93, though heavily transfused, shows no loss of red cells but some loss of plasma protein, that *Case I* 44 shows no loss of protein and a loss of red cells not much above the errors of the methods, and that *Cases I* 74, *I* 78 and *I* 39 show considerable losses of red cells (particularly *I* 74) but smaller losses of plasma protein It is probable that *Case I* 39's blood loss at operation, estimated at 1,200 ml, was even more than this It is clear, however, that operation blood loss fails to account for all the plasma protein and red cells lost during the intervals shown in Section B as well as in Section A Further, the protein losses shown may be underestimates, since it is impossible to estimate the amount of any protein the patient may himself add to his plasma during the interval between the two estimations

Chute *et al* (1945) give similar balance tables for six of their patients with limb injuries which we should probably classify as large In four of these, blood volume estimates were separated by 14–23½ hr and total losses of 320–750 ml. red cells and 23–100 g protein were found Measurements of blood loss at operation were not made These cases were on the average transfused greater quantities than ours

TABLE 49

Repeated blood volume estimations and balance observations: patients with limb injuries

Patient	Injuries	Estimated initial blood loss (per cent predicted normal blood volume)	Interval between 1st and 2nd estimations (hr)		Transfusion before first estimation	First estimation	Gain or loss during interval		Second estimation		Balance	Recalculated red cell balance
							Transfused	Lost		Per cent normal		
				A. Before and after operation (Shorter interval)								
I 49	Moderate	35	3½	Blood volume (ml)		4040	—	—	3330	69	—	—
				Red cell volume (ml)	Nil	1500	—	130	1170	51	−200	−110
				Plasma protein (g)		166	—	14	143	84*	−9	—
I.79	Large	40–45	3½	Blood volume (ml)		3900	—	—	3360	64	—	—
				Red cell volume (ml)	Nil	1520	—	100	1220	49	−200	−120
				Plasma protein (g)		149	—	10	131	74*	−8	—
I 86	Large	35	5	Blood volume (ml)		4250	—	—	4030	70	—	—
				Red cell volume (ml)	Nil	1750	450	190	1590	59	−420	−380
				Plasma protein (g)		169	45	19	160	80*	−35	—
I 76	Large	40	6	Blood volume (ml)		4100	—	—	4280	77	—	—
				Red cell volume (ml)	Nil	1600	300	120	1420	54	−360	−290
				Plasma protein (g)		142	60	12	159	96*	−31	—
I 104	Very large	25–30	6	Blood volume (ml)		3360	—	—	4500	122	—	—
				Red cell volume (ml)	Nil	1430	600	150	1800	103	−80	−150
				Plasma protein (g)		94	60	10	135	135*	−9	—
				B. Before and after operation (Longer interval)								
I.74	Large	25	14	Blood volume (ml)		4720	—	—	4450	81	—	—
				Red cell volume (ml)	Nil	2070	150	100	1560	60	−560	−490
				Plasma protein (g)		146	14	10	160	98*	+10	—
I 44	Moderate	35	17	Blood volume (ml)		3840	—	—	3960	72	—	—
				Red cell volume (ml)	Nil	1670	150	50	1620	66	−150	−130
				Plasma protein (g)		132	14	5	143	79*	+2	—
I.93	Very large	60	20	Blood volume (ml)	—	2940	—	—	4400	86	—	—
				Red cell volume (ml)	70	600	700	50	1340	55	+90	−30
				Plasma protein (g)	60	138	105	10	200	116*	−33	—
I.78	Large	50	20	Blood volume (ml)	Nil	3330	—	—	3640	69	—	—
				Red cell volume (ml)		1260	450	300	1200	49	−210	−185
				Plasma protein (g)		115	70	30	144	86*	−11	—

I 39	Moderate	45	20	Blood volume (ml.)		4360	—	—	3880	67	—
				Red cell volume (ml)	Nil	1520	—	450	720	27	−350	−205
				Plasma protein (g)		172	60	45	170	102	−17	—
C After operation												
I 84	Large	45–50	64	Blood volume (ml)	—	4060	—	—	4390	80	—	—
				Red cell volume (ml)	300	1140	—	—	1030	40	−110	−80
				Plasma protein (g)	80	138	—	—	183	114	+45	—
I 110	Very large	60	64	Blood volume (ml)	—	4200	—	—	5550	97	—	—
				Red cell volume (ml)	1350	1480	300	—	1470	54	−310	−300
				Plasma protein (g)	180	147	60	—	243	134*	+36	—
I 22	Small	30–35	70	Blood volume (ml)	—	4540	—	—	4390	84	—	—
				Red cell volume (ml)	150	1620	—	—	1170	48	−450	−340
				Plasma protein (g)	30	170	—	—	189	117*	+ 19	—
I 88	Large	30	70	Blood volume (ml)		3760	—	—	4800	97	—	—
				Red cell volume (ml)	Nil	1550	—	—	1260	54	−290	−200
				Plasma protein (g)		132	—	—	183	134*	+51	—
I 109	Very large	60	71	Blood volume (ml)	—	3640	—	—	5180	94	—	—
				Red cell volume (ml)	750	850	600	—	1700	66	+250	+45
				Plasma protein (g)	180	171	55	—	236	120*	+10	—
I 58	Moderate	45	72	Blood volume (ml)	—	4220	—	—	4950	93	—	—
				Red cell volume (ml)	750	1630	—	—	1760	70	+130	+120
				Plasma protein (g)	70	192	—	—	228	111	+36	—
I 70	Moderate	45	74	Blood volume (ml)	—	4300	—	—	4900	94	—	—
				Red cell volume (ml)	200	1290	—	—	1090	45	−200	−125
				Plasma protein (g)	50	170	—	—	219	137*	+49	—
I 85	Large	55	81	Blood volume (ml)	—	4130	—	—	4850	86	—	—
				Red cell volume (ml)	600	1160	150	—	1270	48	−40	−80
				Plasma protein (g)	110	145	30	—	218	118*	+43	—

Note The predicted normal post operation blood volumes of patients who at operation lost considerable volumes of their limbs by amputation have been proportionately reduced to allow for the loss of vasculature

*These figures are percentages of the predicted normal *plasma volume*

In Section C are shown the results of similar estimations made after operation and separated by intervals of 64–81 hr. It will be observed that three patients, *Cases I.*58, *I.*84 and *I.*85, show red cell losses or gains within the errors of the methods and one, *Case I.*109, shows a gain of 250 ml. of red cells. This latter gain may be accounted for by transfusions of fresh blood, for which the allowance of 150 ml. of red cells per bottle is probably a 50 ml. underestimate. *Cases I.*22, *I.*70, *I.*88 and *I.*110 showed losses of red cells varying between 200 and 450 ml. All patients showed some gain of plasma protein, varying from 10 to 51 g., which must have been added by their own tissues; it will be noted that *I.*88, who added the greatest quantity of plasma protein, received no transfusion. These observations show that during the first three or four days after operation a number of these patients lost further quantities of red cells. With one possible exception, *I.*109, no patient showed any significant gain of red cells during this period.

Changes in Average Red Cell Volume

The great majority of the mean corpuscular haemoglobin concentrations shown by the patients with limb injuries during the first 72 hr. after injury lay between 31·0 and 35·0 g. per 100 ml. cells: in 140 blood samples drawn from 39 of these patients only 18 exceeded these limits. Six had concentrations ranging from 28 to 30·8 g. per 100 ml. and five of these were drawn from the patient *I.*110 (see p. 33), a Group A recipient who was transfused 12 bottles of Group O blood, which may have accounted for the swelling of his red cells. Six patients, all of whom had been much transfused, showed mean corpuscular haemoglobin concentrations ranging from 35·2 to 39·0 g. per 100 ml., concentrations which indicate a shrinkage of the red cells.

The transfusion of blood, plasma or both might alter the average volume of the recipients' red cells; the red cells of the stored blood were swollen and by our estimates had an average mean corpuscular haemoglobin concentration of about 30·0 g. per 100 ml. We made no observations specifically to examine its effects, but our data indicate that transfusion does not necessarily cause any significant change, although in a number of instances it did appear to result in some increase in this concentration, suggesting that there had been shrinkage of the red cells.

In Table 49 we have reported balance observations derived from paired blood volume estimates and concluded that in a number of instances they indicate losses of red cells. Changes in the average volume of the red cell might affect these balances, for if at the time of the first estimate of total red cell volume the red cells had been 10 per cent greater in volume than at the time of the second, an overestimate of loss of red cells would have resulted. We have therefore examined the mean corpuscular haemoglobin concentrations in each pair of estimates to see if such changes in average red cell volume could account for the observed losses of red cells. In only one patient, *I.*49, is this a possibility, in the others the calculations indicate either no change, or losses rather greater than those shown.

Discussion

Our observations indicate that considerable quantities of red cells and plasma protein may be lost from the circulation of patients with limb injuries after admission to hospital, during the period between admission and operation, during operation, and in the early post-operation period, and that red cells may be lost in the later post-operation period. The estimated losses of

plasma protein derived from the plasma volume estimations and the plasma protein concentrations are probably reliable, although they are too low by the amount of any protein added by the patient himself The estimates of red cell losses are more in doubt We have already pointed out (p 239) that

(1) Our estimates of initial blood loss in individual cases may be considerably in error, in cases estimated to have lost 50 per cent or more of their blood they may tend to be too high, but on the average they are probably not greatly in error

(2) Systematic errors, produced certainly by trapped plasma in the haematocrit and probably by uneven distribution of red cells and plasma in the circulation, on the average make the estimates of blood volume about 10 per cent, and red cell volume about 25 per cent, too great

(3) If there is uneven distribution of red cells and plasma through the circulation, and if there is variation in the percentage of the blood volume occupied by "marginal plasma", then it follows (*a*) that changes in haemoglobin and haematocrit concentration may not exactly reflect changes in the true proportions of total red cells in the total blood volume, and (*b*) that the size of the overestimate of red cell volume, and to a less extent blood volume, may vary at different times

The most important causes of uncertainty are those numbered (2) and (3 *b*)

Dealing first with that numbered (2) to test the effects of the overestimate of total red cell volume given by the dye haematocrit method, all total red cell volume values have been recalculated to give as far as possible the best estimate of "true" total red cell volume by the following formula

$$\text{"true" total red cell volume} = \text{plasma volume} \times \frac{0\ 95 \text{ haematocrit}}{100 - 0\ 95 \text{ haematocrit}} \times 0\ 87$$

The derivation of this formula will be found on p 237 Using revised figures so calculated for total red cell volumes in both first and second blood volume estimates, the red cell balances have been recalculated and are shown in the last column of Table 49 (p 268) It can be seen that this has resulted in most cases in some reduction in the estimated losses of red cells, but in only two cases is this reduction greater than 100 ml Hence the overestimate given by the dye-haematocrit method in the uncorrected form that has been used here probably does not account for the observed loss of red cells

Dealing with (3 *b*) different overestimates by the dye/haematocrit method on different occasions, depending on marked variations in the distribution of red cells and plasma in the circulation, *might* cause apparent losses of red cells of the order found For two important reasons it is unlikely that this has happened First, in Section A it was pointed out that the methods used in determining total red cell volume in states of vasoconstriction might be expected to give an *underestimate* of total red cell volume A number of the first estimates shown were made during periods when there was some vasoconstriction, although this was not gross If the first estimate was low, then the losses of red cells were greater than those indicated Secondly, the independent evidence afforded by the haemoglobin changes supports the findings from blood volume estimations We therefore conclude that the reported losses of red cells are real and not greatly in error

There are few comparable observations by others. From the data published by Keith (1919) the changes in haemoglobin and blood volume of nine cases of skeletal injury can be related to time after injury. Caution must be observed in interpreting the blood volume estimates since an early form of the vital red method was used. In six of these cases, who on the basis of Keith's red cell volume estimates may be calculated to have lost initially 45–65 per cent of their blood, his observations show that by 60 hr. after injury the haemoglobin level had fallen to 30–45 per cent. At this time none of them had been given blood. Blood volume estimations made 30–100 hr. after injury on four of them, after one had been transfused 880 ml. of blood, showed blood volumes varying between 67 and 86 per cent of the predicted normal. These patients differed from ours in having received little or no blood transfusion, but the fall in haemoglobin levels and the persistence of low blood volumes again suggest the loss of more red cells than those lost by the initial haemorrhage. The persistence of low levels of blood volume in the absence of blood transfusion is to be noted.

Dacie and Homer (1946) report observations on cases of limb injury occurring on the Western Front. Their figures showing progressive changes in haematocrit in both limb and abdominal injuries are comparable with the haematocrit changes we observed. Three of their observations on their patients suffering from limb injuries supplement ours: (1) few of their patients showed any significant increase in red cell counts before the sixth day after injury; (2) six out of 20 patients studied had by the fifth day a reticulocyte count of 5 per cent or greater, and their Fig. 7 indicates that such reticulocyte responses were related to red cell counts of 3,000,000 per c.mm. or less; (3) they made a number of observations with the Ashby differential agglutination method of the survival of transfused stored red cells and found no certain evidence that red cells stored for 7–14 days survived less well in battle casualties than in normal recipients. Their observations also suggested that haemolysis of the recipients' red cells of the A, B or AB groups by isoagglutinins in the transfused group O blood did not commonly occur to any great extent.

The possible causes of losses of red cells and plasma in these first few days after injury are:

Loss of whole blood ..	External haemorrhage Haemorrhage into damaged tissues
Loss of red cells only	
(*a*) Patient's	Failure of replacement of normal loss rate of about 1 per cent per day. Removal after reaction with transfused agglutinins or by haemolytic systems Inreased rate of destruction from abnormal metabolism
(*b*) Transfused ..	Removal because imperfectly stored
(*c*) Both	Removal for metabolic needs
Loss of plasma protein only	Passage into tissue fluids Leakage into damaged tissues Removal for metabolism

Bearing in mind the errors of the methods of estimation, the variation in survival of the transfused red cells, and the impossibility of determining the amount of protein added by the patients in the intervals between repeated blood volume estimations, the relative amounts of protein and red cells suggest that in many cases the losses are due to loss of whole blood In a few cases red cell loss is much in excess of plasma protein loss and the most likely explanation is removal of unviable red cells But in Case *I* 74 this explanation will not suffice, since 400 ml more red cells were removed than were transfused Reaction of the patient's red cells with donated plasma iso-agglutinins is a possible explanation

As earlier noted, Table 48 (p 262) shows that a number of patients had failed to restore their blood volumes to predicted normal levels by 3–4 days after injury Table 49 (p 268), Section C, provides further evidence of this, as do Keith's cases quoted above Examination of all the data shows that failure to restore the blood volume levels is due to failure to restore not the plasma volume, which is usually raised to well above normal levels, but the red cell volume, depleted by the initial haemorrhage and the later losses discussed above To restore the blood volumes of such patients to normal levels their red cell volumes must be increased by sufficient blood transfusion

Absence of Haemoconcentration

Haemoconcentration occurs if abnormal amounts of plasma fluid are lost from the circulating blood Such fluid loss can only be established from the analysis of a single sample of blood if the haemoglobin and haematocrit lie above the normal range (In fit troops the normal range of haemoglobin levels may be taken as 100 $\pm$ 12 per cent (= 16 $\pm$ 2g per 100 ml) and haematocrit levels 47 $\pm$ 6 per cent) In patients with normal or reduced haemoglobin and haematocrit levels haemoconcentration can only be established from analysis of serial samples of blood if these show progressive rises in haemoglobin concentration and haematocrit beyond the normal diurnal variations and in the absence of transfusion The above statements need emphasis In the past confusion has arisen because some workers, who have found haemoglobin and haematocrit levels higher than they had expected in the circumstances, have mistaken these for evidence of haemoconcentration

Examination of the initial haemoglobin values given in Fig 8A (p 256) and subsequent values given in Fig 10A, B, C and D (p 264) shows no case with single values above the normal range Examination of the progressive changes in the haemoglobin in Fig 10, and in our other records not illustrated, reveals no case showing a significant rise in haemoglobin during the first four days after injury without considerable blood transfusion The figures, far from providing any evidence of haemoconcentration, show clear evidence of marked and progressive haemodilution

Other authors' findings In limb and skeletal injuries the data on injured soldiers given by Keith (1919), Emerson and Ebert (1945), Chute *et al* (1945) and Dacie and Homer (1946) and the data on injured civilians given by Evans

et al. (1944) and Noble and Gregersen (1946) provide no evidence of haemoconcentration. Thus according to Dacie and Homer the mean haematocrit value of 55 men with "moderate to severe" limb wounds seen 1–7 hr. after injury and before transfusion was 41·2 per cent with a range of 32–49 per cent, and their subsequent courses, shown in their Figs. 5 and 6, give no evidence of haemoconcentration. According to Evans *et al.* (1944) (their Chart 7) the mean haematocrit of 51 untransfused civilian casualties suffering from skeletal trauma seen at short but unstated times after injury was about 40, with a range of 31–49. So it seems that all recent workers agree in finding no evidence of haemoconcentration in these cases.

The writings of some workers have suggested that there is some delay in dilution of the blood in "shock", which may be due to concealed haemoconcentration. If we take our most severely injured patients to have been suffering from "shock", we can find no evidence to support this view.

Conclusions

1. In limb injuries the greatest blood loss occurs at or near the time of wounding.

2. After blood loss there is usually a fairly rapid dilution of the blood, first with protein-free or protein-poor fluid, but later and chiefly with fluid containing protein in nearly the same concentration as the original plasma. During the first 12 hr. after injury the average dilution is roughly proportional to haemorrhage, but there is individual variation.

3. The rate of dilution varies considerably in different individuals. But it can be said that, in fit troops untransfused and seen within 12 hr. of injury in temperate climates, a haemoglobin concentration above 90 per cent (14·4 g. per 100 ml.) indicates a previous blood loss of less than 40 per cent of the blood volume, and a haemoglobin concentration below 75 per cent (12 g. per 100 ml.) a previous blood loss of more than 40 per cent.

4. There is no evidence that in the first 12 hr. the presence of much tissue damage delays the process of dilution.

5. Transfusions of dilute plasma or of stored blood rarely alter the plasma protein concentration by more than $\pm$ 0 5 g. per 100 ml. The major part of the diluent in both rapidly leaves the circulation. Transfusions of much plasma into those who have bled much cause a marked lowering of the haemoglobin. Transfusions of stored blood in considerable amounts tend to bring the haemoglobin to the region of 80 per cent, but when given in conjunction with plasma they bring it to lower levels. Over short periods, and in the absence of further bleeding, a large proportion of the transfused red cells and plasma protein stays in the circulation.

6. Further whole blood loss occurs during operation and in the period immediately after operation.

7. The characteristic later change in haemoglobin concentration is a progressive fall till about the third or fourth day after injury. The rate and extent of the fall are much influenced by the amount of blood lost at wounding and by the quantities of red cells and plasma transfused. Because of the addition of protein to the circulation from the injured subject's tissues, after

the initial reduction the plasma proteins tend to fluctuate about a level near 6 0 g per 100 ml

8 *During the first three or four days after injury more red cells may be* lost, both the patient's own and those transfused Significant quantities of red cells are rarely added by the patient before the fifth day and often not till later

9 *After large haemorrhage, blood volume may remain low for three or* four days after operation and probably often for longer periods The plasma volume increases above normal levels, but the red cell volume remains characteristically low, often in the region of 50 per cent of the predicted normal

10 If these patients are not given sufficient blood, the losses summarized above make them become very anaemic In the first world war, when blood transfusions were given rarely and only in small amount, haemoglobin levels "near 30 per cent" (? 4 8 g per 100 ml) were not uncommon and were associated with low blood volumes In the last war, in spite of much transfusion, haemoglobin levels of 50–60 per cent (8–9 6 g per 100 ml) were not uncommon by the fourth to sixth day after large haemorrhage, and again were often associated with reduced blood volumes

11 Limb and skeletal injuries show no evidence of haemoconcentration at any stage of their course

ABDOMINAL INJURIES

It might be expected that the changes in haemoglobin and plasma protein concentration and in the volume of plasma and red cells occurring in patients with limb injuries would also occur in patients with abdominal injuries who have lost similar amounts of blood This is in large part true There were, however, certain important differences which might modify the picture seen First, patients with abdominal injuries, particularly when the intestine was perforated, were liable as a result of vomiting, treatment by indwelling gastric suction, and other causes to suffer from disturbances of salt and water metabolism culminating in dehydration Secondly, they were liable to develop septic infections additional to those from which patients with limb injuries suffered, particularly in the lungs and peritoneum The changes shown by their blood are examined below and compared with the changes already described in patients with limb injury, paying chief attention to the differences shown

In Part II patients with abdominal injury have been divided into (*a*) those in whom there was no intraperitoneal perforation of the intestine and (*b*) those in whom there was perforation Either type might be combined with injury elsewhere, though in the majority of cases dealt with in this section the other injuries were not great Further details of our cases will be found in Part II Data taken from the cases of Keith (1919), Emerson and Ebert (1945) and Chute *et al* (1945) are also used Six of the cases of Chute *et al* later quoted may have had other wounds which we should classify as large, we should probably classify the other cases of the above authors, from the descriptions given, as having moderate or small wounds

Early Blood Changes and their Interpretation

Untransfused Patients

In Figs. 8A and B (p. 256) are plotted the initial levels of haemoglobin and plasma protein of 12 untransfused cases of abdominal injury without intestinal perforation. It can be seen that these levels are related to estimated initial blood losses as in patients with limb injuries, so that the same deductions about dilution, etc., can be made.

All but a few of those with perforating intestinal injuries had already been transfused when we first saw them, so for these patients we ourselves have few pre-transfusion observations. Keith (1919), Emerson and Ebert (1945) and Chute *et al.* (1945), however, report pre-transfusion estimations of haemoglobin and plasma protein concentrations and blood volume (Keith gives no plasma protein concentrations). In Fig. 12 the initial haemoglobin and plasma protein levels of the patients described by the above workers, and of the few seen by ourselves, are plotted against the initial blood losses as estimated from blood volume figures. The values shown in Fig. 12 may be compared with those shown by patients with limb injury and plotted in Fig. 8. Fig. 12 shows observations on only one patient estimated to have lost more than 40 per cent of his blood, and complete observations on five estimated to have lost between 21 and 40 per cent; the haemoglobin and plasma protein levels of these patients do not differ significantly from those of patients with limb injuries who suffered similar blood loss (Figs. 8A and B). It is otherwise when blood loss is 20 per cent or less. While plasma protein levels are, with two exceptions, in the same range as those of patients with limb injuries, haemoglobin concentrations range from 90 to 115 per cent and haematocrits from 42 to 54 per cent; i.e. rather more than half of the haemoglobin and haematocrit values lie above those of patients with limb injury, but none below, which suggests that perforating intestinal injuries with little blood loss are sometimes accompanied by haemoconcentration.

This section may be summarized thus. There is no evidence to suggest that patients with abdominal injury not perforating the intestine, or those with intestinal perforation who have lost more than 20 per cent of their blood, dilute their blood differently from patients with limb injury suffering equivalent losses. There is evidence that some patients with intestinal penetration and a blood loss of less than 20 per cent have haemoglobin levels higher than those with limb injury and equivalent blood losses.

Transfused Patients with Perforating Intestinal Injuries

Many of the patients with intestinal penetration were given transfusions of plasma and some blood soon after injury and before being seen by us. The effects of such transfusions are therefore now examined. In Fig. 13 are plotted the concentrations of haemoglobin and plasma protein of such patients after transfusion. To supplement our own observations we have included similar observations taken from Emerson and Ebert (1945) and Chute, Cleghorn and Armstrong (1945), estimating initial blood loss from the published blood volume figures. The majority of patients shown in Fig. 13 had been

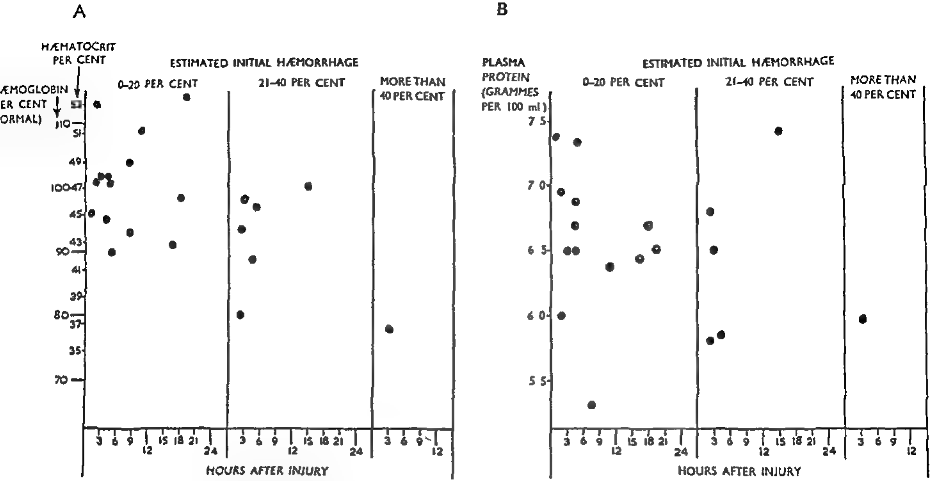
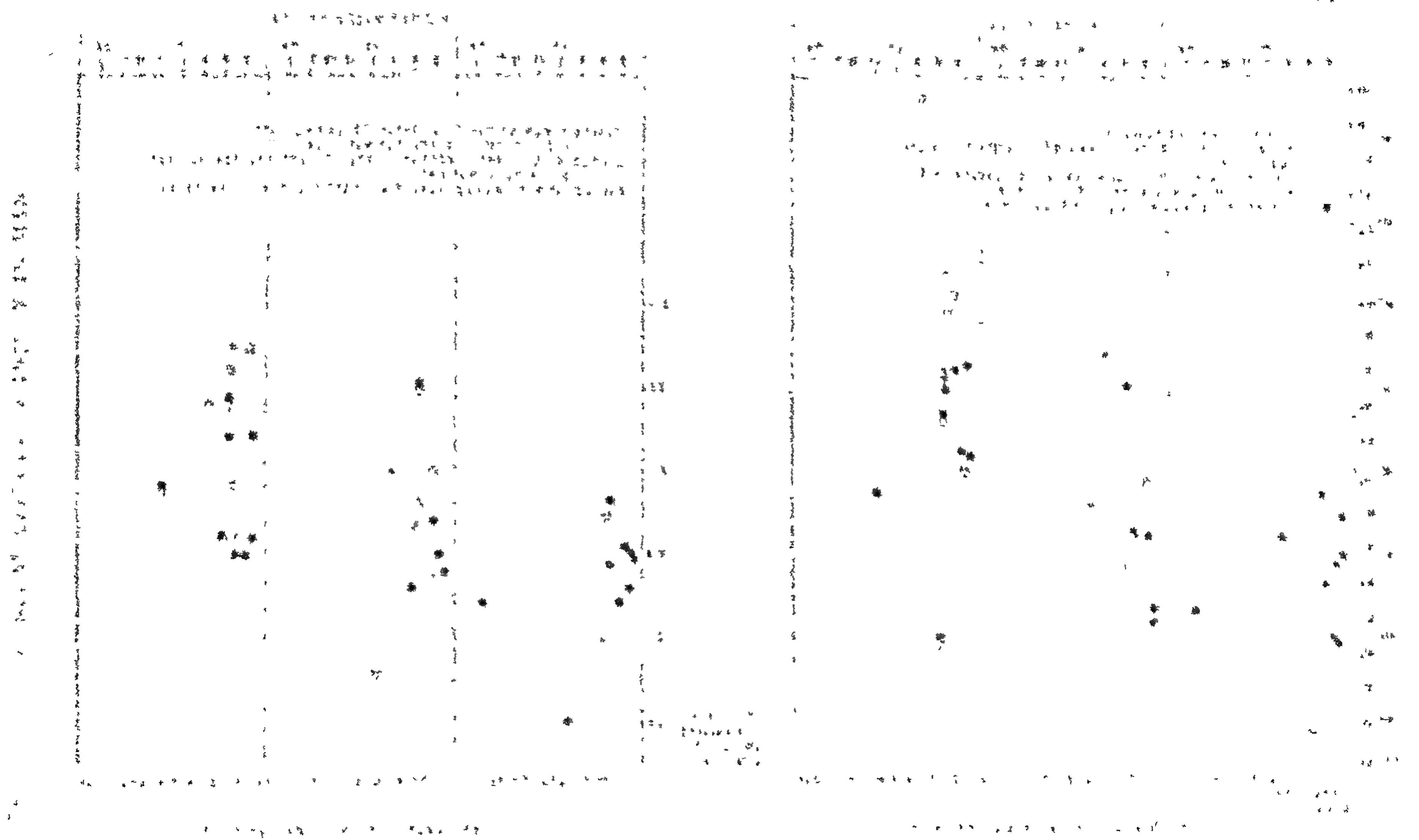


FIG 12 (A) Initial haemoglobin and (B) plasma protein concentrations in untransfused patients with abdominal injuries penetrating the intestine

Data taken from cases nos 25, 36 and 44 of Emerson and Ebert (1945), nos 23 119, 124, 125, 146, 148 and 156 of Chute *et al* (1945) cases W B and G W W of Keith (1919) (no plasma protein concentrations given) and from *our own observations*



transfused with plasma, but nine had received two or three bottles of blood with or without plasma, the approximate quantities of plasma are indicated, and, since different workers used different preparations of plasma, to secure uniformity of presentation the amounts transfused are shown in terms of ml of a solution of 6 g protein per 100 ml These quantities were obtained by dividing the total grammes of protein transfused by 6 and multiplying by 100 In the majority of cases more dilute solutions than this were transfused, but it can be seen in Fig 13B that the plasma remaining in the circulation had a protein content of about 6 g per 100 ml

Plasma transfusion We will first consider those patients transfused with plasma Reporting all values in terms of haemoglobin per cent, the haemoglobin values (Fig 13) during the first 12 hr after injury lay between 79 and 100 per cent in those estimated to have lost 20 per cent or less of their blood, between 66 and 98 per cent in those estimated to have lost 21–40 per cent of their blood, and between 35 and 78 per cent in those estimated to have lost more than 40 per cent of their blood In each group the lower levels of haemoglobin are associated with greater plasma transfusions

Approximate calculations can be made of the reductions in haemoglobin concentration that would be expected after transfusions of given quantities of plasma to patients with given blood losses, and these may be compared with the values observed An average patient may be taken before wounding to have a blood volume of 5,500 ml and a haemoglobin concentration of 100 per cent. Neglecting any spontaneous dilution by the patient, an initial blood loss of 30 per cent of the blood volume will reduce the blood volume to 3,850 ml , the addition of 500 ml of plasma will increase it to 4,350 ml and reduce the haemoglobin concentration to about 88 per cent, while 1,000 ml of plasma will increase it to 4,850 ml and reduce the haemoglobin concentration to about 79 per cent Similarly, transfusions of 500 ml of plasma to a patient who has initially lost 50 per cent of his blood will reduce the haemoglobin concentration to about 85 per cent, and 1,000 ml of plasma to about 73 per cent Any additional spontaneous dilution will result in lower levels of the haemoglobin than those calculated

Fig 13 divides the patients according to whether they received less than 600 ml , 600–1,200 ml , or more than 1,200 ml , of plasma with a protein content of 6 0 g per 100 ml Excluding from the patients of the centre column of Fig 13A those who were transfused blood, those who received plasma transfusions of less than 600 ml had a mean haemoglobin concentration of about 88 per cent (range 70–98) and those who received 600–1,200 ml a concentration of about 80 per cent (range 74–83) Since the mean haemorrhage for these patients was 30 per cent, these results may be compared with the calculations of the haemoglobin reduction given above for patients losing 30 per cent of their blood and transfused 500 ml or 1,000 ml plasma, and it will be seen that the mean values are very close to those calculated This suggests that either spontaneous dilution was reduced, or some of the transfused plasma left the circulation

Of the patients shown in the right hand column of Fig 13A, those who received plasma transfusions of less than 600 ml had a mean haemoglobin

concentration of about 72 per cent (range 67–78), and those who received 600–1,200 ml. a mean concentration of about 53 per cent (range 35–61). Since the mean haemorrhage here was 50 per cent, these results may be compared with the calculations for patients losing this proportion of their blood and transfused 500 ml. or 1,00 ml. plasma. In both cases the observed mean haemoglobin concentrations are well below those calculated, indicating that in these cases also spontaneous dilution had taken place.

The plasma protein concentrations of these patients are shown in Fig. 13B. In those estimated to have lost 20 per cent or less of their blood they lie between 6·2 and 7 5 g. per 100 ml., in those estimated to have lost 21–40 per cent of their blood between 5·5 and 7·2 g. per 100 ml., and in those estimated to have lost more than 40 per cent between 5·4 and 6·5 g. per 100 ml. There is no close correlation between the quantity of plasma transfused and the plasma protein concentration, but on the average the greater the initial haemorrhage the lower the concentration. The plasma transfused to many of the cases had a protein content of about 4·0 g. per 100 ml. The plasma protein concentrations shown in Fig. 13B indicate, as already noted, that in the majority of cases the transfused plasma was retained in the circulation in a concentration of near 6 g. protein per 100 ml. and that the crystalloid diluent soon left the blood.

Blood transfusion. The patients given blood would be expected to have haemoglobin levels rather higher on the average than those transfused with plasma alone, but to have plasma protein levels in the same range. In practice these generalizations are found to be roughly true. Thus those of the patients estimated initially to have lost 21–40 per cent of their blood who were transfused two or three bottles of blood had haemoglobin concentrations higher than those transfused more than 600 ml. of plasma (containing more than 36 g. protein). Similarly, three out of five of those estimated to have lost more than 40 per cent of their blood and given two or three bottles of blood had haemoglobin concentrations above those of the patients who had received plasma only, while the patient with the lowest haemoglobin concentration who had received blood had also received more than 1,200 ml. of plasma (protein content 6 g. per 100 ml.). One patient transfused blood and estimated to have lost less than 20 per cent of his blood shows the only haemoglobin value much above 100 per cent.

This section may be summarized thus. Patients with perforating intestinal injury who are given plasma soon after injury retain the protein in their circulation in a concentration of about 6 0 g. protein per 100 ml. After transfusion of plasma, those who have lost 21–40 per cent of their blood show haemoglobin diluted by about the expected amounts, suggesting either reduction of spontaneous dilution or loss of some transfused protein, but in those who have lost more than 40 per cent it is diluted by more than the expected amounts, indicating that blood volume has been further increased by spontaneous dilution. As expected, transfusions of blood and plasma result in higher haemoglobin levels but the same plasma protein levels as transfusions of plasma only.

Haemoconcentration

In patients with abdominal injuries during the first 12 hr after injury and before transfusion there are two processes that can result in concentration of the blood (*a*) loss of salt solution (dehydration), for instance as a result of vomiting, (*b*) loss of protein-containing solution, for instance by plasma leakage into an inflamed peritoneum Whereas dehydration will result in a rise in both haemoglobin and plasma protein, leakage of protein-containing solution will result in a raised haemoglobin but a normal or low plasma protein concentration

We have already noted that the haemoglobin concentrations of some of the untransfused patients with intestinal perforation estimated to have lost 20 per cent or less of their blood (Fig 12A, p 277) suggest some slight degree of haemoconcentration, though only two patients had a concentration above the limits earlier defined Those in whom the concentration was more than 100 per cent had plasma protein concentrations of 6 0–7 3 g per 100 ml In only one, *Case* 44 of Emerson and Ebert, did the association of a plasma protein concentration of 6 0 g per 100 ml with a haematocrit of 53 5 per cent indicate definitely the loss of protein-containing fluid from the circulation, the decrease in the plasma volume of the rest was probably due to dehydration

A third possible cause of haemoconcentration is excess blood transfusion Fig 13A, p 278, shows the haemoglobin concentrations of similar patients after they had been transfused, only one had a haemoglobin concentration above 100 per cent, and he had received three bottles of blood and was estimated initially to have lost less than 20 per cent of his blood It seems probable that the blood transfusion was at least partly responsible for the raised haemoglobin

From these observations it is clear that in the first 12 hr after injury pronounced haemoconcentration is not common in those suffering penetrating intestinal injuries Further evidence supports this statement. Dacie and Homer (1946, their Fig 2) report haematocrit observations on 28 injured soldiers suffering from penetrating intestinal injuries seen 1–5 hr after injury Only four of these had haematocrits above 50, the approximate values being 51, 52, 53, and 54 per cent no estimates of haemorrhage or plasma protein concentrations are given Of 31 abdominal injuries in civilian casualties reported by Evans *et al* (1944), seen at short but unspecified times after injury and not transfused, only five had haematocrits over 50, of these, three suffered from ruptured intestines (two with ruptured jejunum, one with ruptured ileum), one from ruptured bladder and peritonitis, and one from unstated injuries due to gunshot wound The haematocrit values, plasma protein concentrations, and initial haemorrhages estimated from the plasma volume and haematocrit observations given, stated in that order, were as follows 51 per cent, 7 2 g per 100 ml, blood loss 35 per cent, 54 per cent, 7 2 g per 100 ml, blood loss nil, 55 per cent, 5 6 g per 100 ml, blood loss 17 per cent, 57 per cent, ? g per 100 ml, blood loss 5 per cent, 60 per cent, 7 3 g per 100 ml, blood loss 23 per cent The estimates of initial haemorrhage may be too high, and are probably less reliable than those made for battle casualties The high protein values in three of the four cases suggest that dehydration was the chief cause of the raised haemoglobin

Where much blood has been lost it is possible that the normal process of dilution, which consists of increasing the plasma volume by the addition of new and rather more dilute plasma, may be impeded, either from shortage of tissue fluids required for dilution, or by escape of newly added plasma into inflamed tissues. There are too few observations on those who had bled much and were untransfused when first seen to establish whether or not this occurs during the first 12 hr. after injury. The few observations in Fig. 12 on those who lost 21–40 per cent of their blood suggest that, in these patients at least, dilution proceeded as in those with limb injuries shown in Fig. 8 who

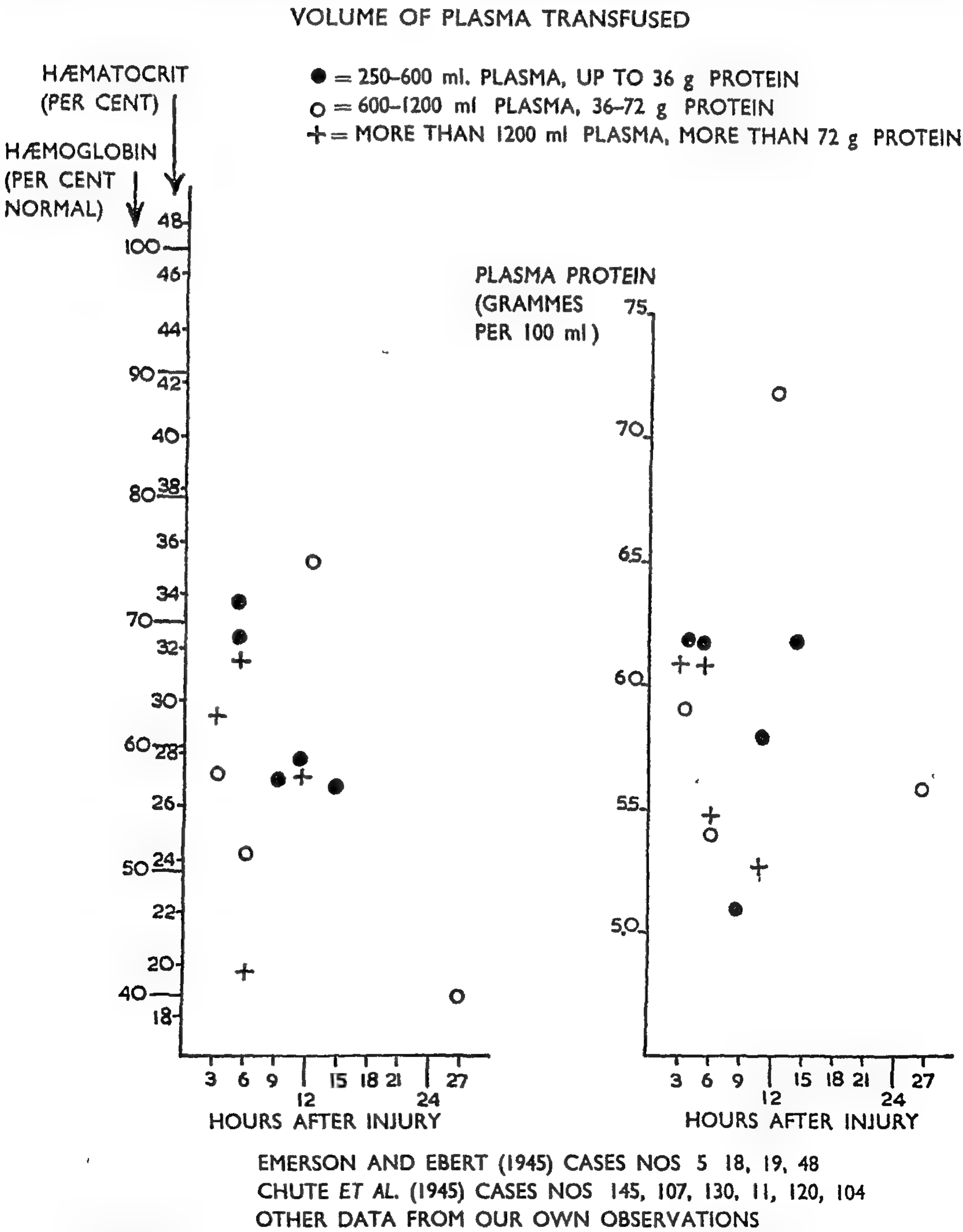


FIG 14. Initial haemoglobin and plasma protein concentrations, after plasma transfusion, in patients with limb injuries who are estimated to have lost over 40 per cent of their blood

were estimated to have lost initially equivalent amounts of blood In Fig 13 are shown observations on nine patients who lost more than 40 per cent of their blood and were transfused 250–1,200 ml of plasma In Fig 14 are shown, for comparison, similar observations on cases of limb injury taken from Emerson and Ebert (1945), Chute *et al* (1945) and from our own records, who lost similar amounts of blood and were also transfused plasma, the amounts transfused (250–1,200 ml) are indicated in the same manner as in Fig 13 The two figures show that in the patients with abdominal injury most of the haemoglobin values lie between 55 and 80 per cent, and in the patients with limb injury between 50 and 75 per cent If the errors in the methods used by the three different groups of observers are remembered this indicates little difference between the two types of injury in the process of dilution after great haemorrhage, when this process is assisted by transfusions of plasma The two ranges of plasma protein concentration are also close to each other

This section may be summarized thus pronounced haemoconcentration rarely occurs during the first 12 hr after injury in those suffering from penetrating intestinal wounds, smaller degrees of haemoconcentration do occur, and are probably most often due to dehydration, evidence is insufficient to show whether after haemorrhage processes tending to haemoconcentration may interfere with spontaneous haemodilution, but it appears that they do not always interfere, and that they do not interfere with the haemodilution caused by plasma transfusion

Practical Rules

From the data given in Figs 12 and 13 certain practical conclusions may be drawn

In untransfused patients with abdominal injury first seen during the first 12 hr after injury it is probable that a haemoglobin concentration of 105 per cent or a haematocrit of 49 per cent or above indicates a blood loss of less than 20 per cent of the total blood It is almost certain also that two of the rules adduced for the limb injuries can also be applied to such cases (1) that a haemoglobin concentration below 75 per cent (12 g per 100 ml , haematocrit 35 per cent) indicates haemorrhage of more than 40 per cent, (2) that a haemoglobin concentration of 75–85 per cent (12–13 6 g per 100 ml , haematocrit 35–40 per cent) indicates haemorrhage of 20 per cent or over

In cases transfused 600–1,200 ml of plasma (containing 36–72 g protein) a haemoglobin concentration below 65 per cent almost certainly indicates haemorrhage greater than 40 per cent In cases transfused less than 600 ml of such plasma a haemoglobin concentration near 75 per cent strongly suggests haemorrhage of more than 40 per cent Again these rules only apply to fit troops and might not apply in very hot or very cold climates

Effects of Transfusion on Blood Dilution

The remarks already made under this heading for the limb injuries apply also to the abdominal injuries Attention is drawn to the observations of

Emerson and Ebert (1945) quoted in Table 45 (p. 247), which indicate that a large proportion of the transfused red cells and plasma protein can remain in the circulation over short periods of time and that in general the transfusion of large quantities of dilute plasma to these cases causes little alteration to the plasma protein concentration.

The Course of Blood Dilution and its Interpretation

In *patients without perforation of the intestine* and not treated with indwelling intragastric suction, the changes during the first five days after injury in both haemoglobin and plasma protein concentrations, when related to estimated initial blood losses, were closely similar to those in patients with limb injuries. The estimated initial haemorrhage did not account for the total loss of red cells indicated by the fall in haemoglobin levels.

The changes in *patients with perforating intestinal injuries* are shown in Figs. 15 and 16. Those estimated to have lost initially not more than 10 per cent of their blood are dealt with in Section A of each figure. The amounts of red cells and plasma protein transfused are indicated as in Figs. 10 and 11. It will be observed that a number of these patients showed falls of haemoglobin to levels of 70 per cent by the fifth day after injury, so again the estimated initial haemorrhage cannot account for all the red cell losses indicated by the fall in haemoglobin. Patients estimated to have lost 40–50 per cent of their blood are shown in Figs. 15B and 16B. Though all cases had received four or five bottles of blood and one had received seven bottles, by the third day the average haemoglobin level was about 70 per cent. From evidence presented in the next paragraph it is probable that most, if not all, had blood volumes reduced well below their predicted normal levels, which when taken in conjunction with the haemoglobin values again suggests greater losses of red cells than those estimated to have occurred at wounding. In this group, with one exception, the plasma protein levels were 6·0 g. per ml. or more from the second day onwards and all received considerable quantities of protein by transfusion. Taking the mean haemorrhage to be 50 per cent it can be seen that all these patients received more protein than required to raise the plasma volumes to the levels achieved.

Balance Observations

Table 50 shows the results of a number of repeated blood volume estimations on abdominal injuries, 50A those without, and 50B those with intestinal perforation. All but two estimations were made after operation and the pairs were separated by intervals varying from 72 to 330 hr. Brief descriptions of the injuries, the estimated initial blood losses, and the transfusion before the first estimation and between this and the second are given, with balances calculated as described for Table 49.

Section A of the table shows that only the two patients estimated to have lost initially less than 20 per cent of their blood had blood volumes which at the time of the second estimation reached the predicted normal levels, and one of these had been given much plasma. The second blood volume estimations of the remainder range between 78 and 91 per cent of the predicted

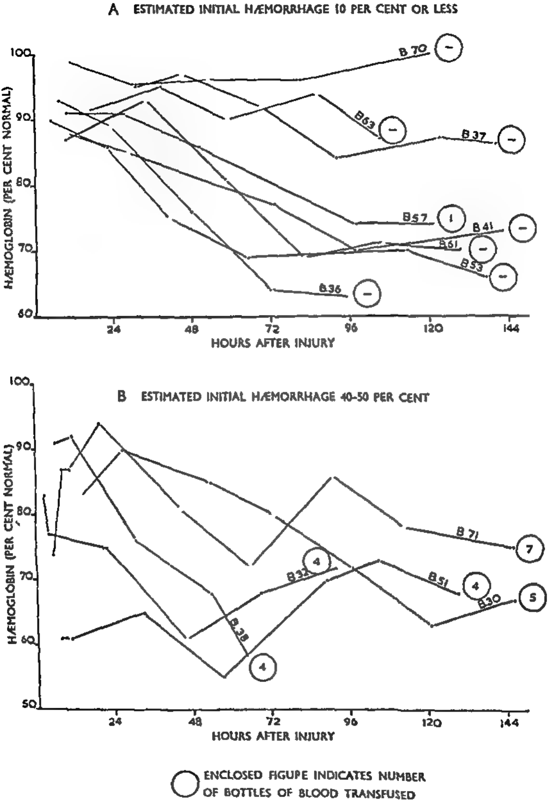


FIG 15 Haemoglobin changes in patients with abdominal injuries penetrating the intestine

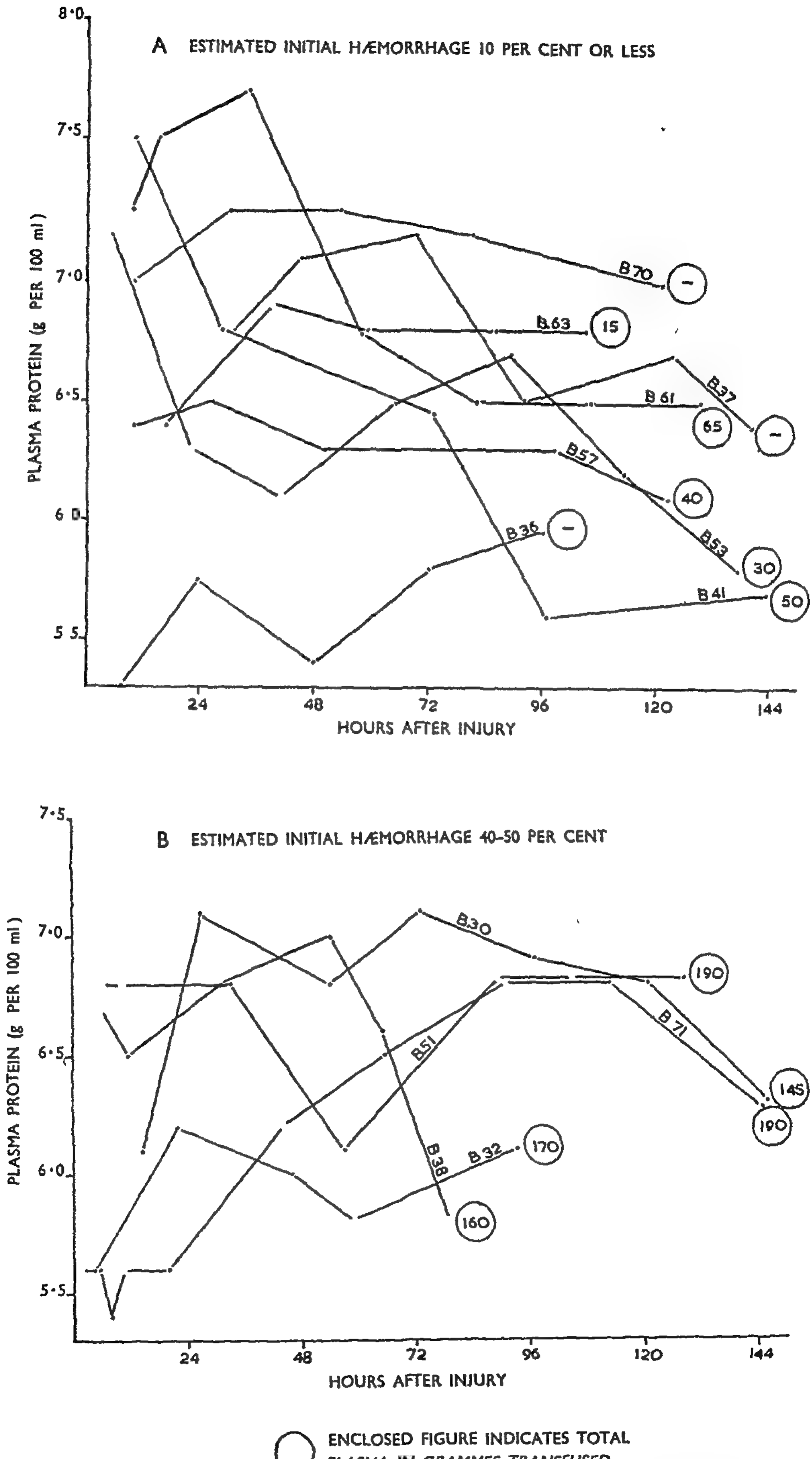


FIG. 16. Plasma protein changes in patients with abdominal injuries penetrating the intestine

normal In all but one case the second estimate of total red cell volume is low, ranging from 36 per cent to 70 per cent of the predicted normal, and balance observations suggest, with one exception, losses of 120–260 ml red cells between the two estimations, revised balance values calculated as for Table 49 (p 268) show losses of 80–190 ml No case was given red cells between the two estimations and none showed any gain of red cells These losses are of about the order expected if the red cells present at the first blood volume estimation had been removed at their normal rate (about 1 per cent per day) and no new ones had been formed In all instances the plasma volume had, by the time of the second blood volume estimation, been restored to predicted normal or a maximum of 26 per cent above Thus these patients, like those with limb injury, may show further losses of red cells after operation In two respects they differed from patients with limb injuries five out of seven developed lung infections and four were treated with continuous intragastric suction for four days

In Table 50B are shown similar observations on patients with perforating intestinal injuries, five of whom are estimated to have lost 10 per cent or less of their blood, the other five 40 per cent or more The first blood volumes in the first two of these cases were estimated before operation, but at operation little blood was lost In the others all the estimations shown were made after operation

Of the five patients losing 10 per cent or less of their blood, only one of whom received a blood transfusion, all showed considerable losses of red cells over periods of 112–220 hr The estimates of these losses range from 320 to 670 ml, and the recalculated estimates from 200 to 450 ml The second blood volume estimation was close to or above normal in all five, but the red cell volume was reduced to levels of 69–86 per cent of normal and the plasma volume was raised above normal, ranging from 115 to 134 per cent of predicted normal One, *Case B* 48, showed a loss of 40 g of protein, equivalent to 670 ml of plasma, while *Case B* 36 showed a gain of 83 g, equivalent to about 1,400 ml of plasma The other cases showed only small gains or losses

Only two of the five losing 40 per cent or more of their blood were found at the second blood volume estimation, made 95–160 hr after the first, to have blood volumes near normal and both of them had been much transfused The other three, although one had been transfused considerable quantities of red cells and plasma, had blood volumes of 80–88 per cent of predicted normal At this time red cell volumes were much reduced, ranging from 35 to 71 per cent of the predicted normal volume, whereas plasma volumes ranged from near normal to 135 per cent of normal Balance observations show a marked loss of red cells in only one case (650 ml), a considerable gain of 47 g protein (equivalent to about 800 ml of plasma) in *B* 58, and losses of 11–75 g of protein, equivalent to 200–1,200 ml of plasma, in the other cases All but one patient in Table 50B had a lung infection or peritonitis or both, all were treated by continuous intragastric suction for several days and received a very low calorie intake (see p 169), and four were certainly suffering from disturbances of salt and water metabolism

TABLE 50

Repeated blood volume estimations and balance observations in patients with abdominal injuries

Patient	Injuries	Estimated initial blood loss (per cent predicted normal blood volume)	Interval between 1st and 2nd estimations (hr)		Transfusion before first estimation	First estimation	Gain or loss during interval		Second estimation		Balance	Recalculated red cell balance	Notes
							Transfused	Lost		per cent normal			
				A Patients without intraperitoneal perforation									
B 18	Severe bruise of upper jejunum	10 or less	140	Blood volume (ml)	Nil	5200	—	—	5420	113	—	—	Lung infection
				Red cell volume (ml)		2580	—	—	2330	103	−250	−140	
				Plasma protein (g)		168	—	—	187	121*	+19	—	
B 17	Pneumothorax and haemothorax, bruise of the ileum	10–20	100	Blood volume (ml)	—	4950	—	—	5550	100	—	—	4 days on intragastric suction, lung infection
				Red cell volume (ml)	150	1980	—	—	1760	67	−220	−170	
				Plasma protein (g)	20	197	90	—	260	126*	−27	—	
B 20	Bruised terminal ileum, retroperitoneal haematoma through-and-through wound of rectum	30	115	Blood volume (ml)	Nil	3540	—	—	4070	89	—	—	
				Red cell volume (ml)		1430	—	—	1200	58	−230	−170	
				Plasma protein (g)		136	36	—	161	120*	−11	—	
B 10	Hole through pleura, diaphragm, spleen and retroperitoneal tissues	30+	115	Blood volume (ml)	—	4790	—	—	4750	91	—	—	Lung infection
				Red cell volume (ml)	150	1820	—	—	1700	70	−120	−140	
				Plasma protein (g)	30	179	—	—	188	105*	+9	—	
B 2	Broken rib, wounds of abdominal wall and right thigh	30+	100	Blood volume (ml)	—	4350	—	—	4080	78	—	—	4 days on intragastric suction, lung infection
				Red cell volume (ml.)	150	1340	—	—	1080	44	−260	−190	
				Plasma protein (g)	70	191	—	—	171	107*	−20	—	
B 8	Hole in liver	30–40	330	Blood volume (ml)	—	4300	—	—	4570	88	—	—	4 days on intragastric suction
				Red cell volume (ml)	300	1330	—	—	1310	54	−20	−10	
				Plasma protein (g)	45	174	—	—	209	117*	+35	—	
B 1	Retroperitoneal haematoma	40+	72	Blood volume (ml)	—	3550	—	—	4560	82	—	—	4 days on intragastric suction, lung infection
				Red cell volume (ml)	—	1090	—	—	960	36	−130	−80	
				Plasma protein (g)	30	146	70	—	193	122*	−23	—	

B Patients with intraperitoneal perforation

B 48	5 holes in small intestine	10 or less	116	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	Nil	5640+ 2920 173	— — 90	— 70 7	5580 2180 216	95 71 117	— −670 −40	— −430 —	4 days on intragastric suction lung infection salt shortage
B 57	Pelvic colon almost severed peritonitis	10 or less	112	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	— 150 20	5360+ 2360 170	— — 18	— — —	4980 1800 184	96 74 115	— −560 −4 (? operative blood loss)	— −450 —	3 days on intragastric suction lung infection
B 36	Through and through wound of upper jejunum	10	220	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	Nil	4900 2200 141	— — —	— — —	5750 1880 224	102 71 125	— −320 +83	— −200 —	4 days on intragastric suction lung infection peritonitis
B 53	Through and through wound of splenic flexure	10	170	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	Nil	5200 2300 171	— — 30	— — —	5960 1840 204	101 69 132*	— −460 +3	— −340 —	3 days on intragastric suction lung infection peritonitis salt shortage
B 61	Through and through wound of liver and hepatic flexure	10 or less	140	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	— — 18	5700 2730 206	— — 48	— — —	6280 2260 216	113 86 134	— −470 −8	— −350 —	3 days on intragastric suction lung infection
B 29	Through and through wound of stomach and liver	40	100	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	— — 60	4330 1270 215	— — 45	— — —	4400 1280 185	80 50 104	— Nil −75	— +10 —	? Lung infection ? Salt shortage 3 days on intragastric suction
B 30	Through and through wounds of pleura, spleen and stomach	45	120	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	— 750 140	5540 2200 209	— — —	— — —	5000 1550 198	88 59 112	— −650 −11	— −490 —	3 days on intragastric suction very hot weather lung infection ? salt shortage
B 62	Holes in transverse colon caecum and liver haemothorax	50	160	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	— 300 90	4200 1180 179	— 600 100	— — —	5900 1870 248	102 68 135	— +40 −31	— −60 —	5 days on intragastric suction lung infection salt shortage
B 51	Perforated bladder fractured ilium and pubis	50	140	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	— 200 110	3920 1140 181	— 550 90	— — —	5200 1770 231	98 71 120	— +80 −40	— −60 —	6 days on intragastric suction salt shortage lung infection peritonitis
B 58	Through and through wound of caecum large tissue damage	50+	95	Blood volume (ml.) Red cell volume (ml.) Plasma protein (g.)	— 300 105	3180 840 135	— — —	— — —	3980 820 182	80 35 119	— −20 +47	— −20 —	3 days on intragastric suction lung infection

Note All the first estimates of blood volume were made within 24 hr of injury Only two marked with a +, were made before operation, all the rest after
*These figures are percentages of predicted normal *plasma volume*

Discussion

In the above observations the first point to be noted is the fall in haemoglobin that may occur in those with penetrating intestinal injuries who initially lost little blood. Operative blood loss did not account for this, and a number of these cases received no transfusion of blood. The blood volume and balance observations shown in Table 50B indicate that an important cause of these falls was further losses of red cells, often of considerable volume; for instance, *Case B*.48 lost the red cell equivalent of 1,000–1,500 ml. of his blood. From the brief clinical notes given it is apparent that a high proportion of all the abdominal cases shown in Table 50 suffered from infections in their lungs or elsewhere, and for several days were treated with intragastric suction, so that their salt and water metabolism was disturbed; these factors must be added to those listed on p. 272 as possibly causing these red cell losses in limb injuries. In Section G it is also shown that many of these patients received for periods of some days after operation a very inadequate calorie intake, and this semistarvation may have been an additional factor.

The later reduction in and restoration of blood volume. The results in Table 50 and the analysis given shows that failure to restore the blood volume to normal or near-normal levels by 5–10 days after injury was due, as in patients with limb injury, to failure to replace red cells lost by haemorrhage or in other ways. In all cases plasma volume was restored to normal or supranormal levels. *Cases B*.51 and *B*.62 show that to restore blood volumes to normal levels after much loss of red cells a large volume of red cells must be transfused.

Later Haemoconcentration

We have seen that in the earlier stages haemoconcentration can arise in three ways: (*a*) by loss of protein-containing solution from the plasma, (*b*) by loss of salt solution from the plasma, and (*c*) from excess blood transfusion, and that causes (*a*) and (*c*) are rare. The situation in the later stages is similar.

Loss of protein-containing fluid from the plasma. This was only apparent in two cases.

Case B.34 (see p. 166), suffering from a penetrating wound of the abdomen through which his intestines protruded, with a large tear in the ileum and a hole in the jejunum, had when first seen after injury a haemoglobin concentration of 109 per cent and a plasma protein concentration of 6 0 g. per 100 ml. After operation and the transfusion of 800 ml. of blood (which roughly replaced the blood found in his peritoneum at operation) blood volume estimation showed the red cell volume to be 96 per cent but the plasma volume to be only 76 per cent of the predicted normal. His haemoglobin was then 109 per cent and his plasma protein 6 2 g per 100 ml He died a few hours later, after he had been transfused a further bottle of blood and two bottles of plasma, and at necropsy was found to be suffering from an early generalized peritonitis, with oedema of the mesentery and perirenal tissues and some excess fluid in the peritoneum.

Case B 31 (p. 163), who had tears in his liver, stomach and spleen and a haemothorax, and had probably lost at least a litre of blood, was transfused 2,000 ml. of whole blood. Postoperatively his haemoglobin level was 124 per cent (19 8 g.), his plasma protein 6 8 g. per 100 ml, his total red cell volume 90 per cent and his plasma volume 58 per

cent predicted normal He died one hour after the blood volume estimation and necropsy revealed fibrino-purulent peritonitis

It is probable that these two are instances of leakage of plasma into inflamed tissues In such cases it would be expected that the plasma protein level would be at or below normal levels, but the haemoglobin level raised

Salt loss from plasma Fig 17 shows the changes occurring in the haemoglobin, plasma protein, plasma bicarbonate and plasma chloride of *Cases B* 51 and *B* 39 during the development of salt deficiency subsequently treated

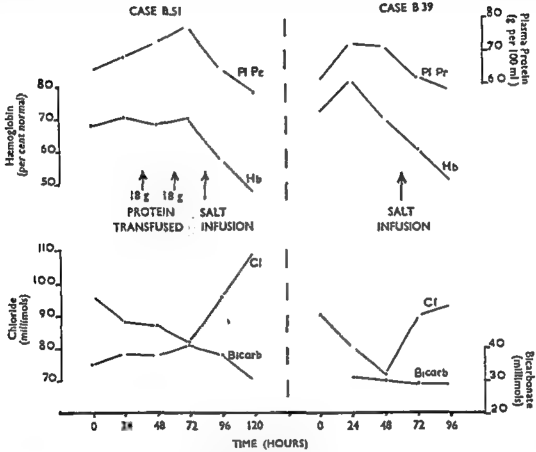


FIG 17 Effects of salt shortage on blood concentrations

Time scale For B 51, 0 hr = 130 hr after injury
„ B.39, „ = 30 „ „ „

with salt infusions (for further details see pp 300 and 306) In each case the chief cause of the disturbance in salt metabolism was the removal of gastric and intestinal juices by intragastric suction The extent of the salt deficiency is roughly indicated by the level of the plasma chlorides

In *Case B* 51, during the first three days shown, the haemoglobin concentration changed little but the plasma protein concentration rose This rise was complicated by the transfusion during this period of plasma containing about 36 g protein On the restoration of salt and water balance by infusion of much salt solution, both haemoglobin and plasma protein levels fell considerably (This case is further discussed in Section G, p 300)

Case B 39 had no transfusions of blood or plasma over the period shown During the first three days, while the salt deficiency was developing, there was first a rise and

then a fall in haemoglobin concentration, with a maintained rise of plasma protein concentration. After the infusion of much saline a marked fall in both haemoglobin and plasma protein levels occurred.

These cases are presented as the two we saw that best illustrate the changes in blood concentration caused by disturbances of salt and water metabolism. Changes as well marked as this were rarely seen. The effects of these disturbances are discussed on p. 297.

Over-transfusion. One patient with abdominal wounds lost at most 25 per cent of his blood and subsequently developed high haemoglobin levels because of much blood transfusion.

Case B 69, who had 12 holes in the small intestine and 2 in the pelvic colon and moderate limb wounds, was transfused 3,600 ml. of whole blood (nine bottles of blood). His haemoglobin rose to 145 per cent (23·3 g. per 100 ml.) and his plasma protein remained at 6 5 g. per 100 ml. At the end of this transfusion blood volume estimation showed his red cell volume to be 136 per cent and his plasma volume to be 79 per cent of predicted normal. He died two days later and at necropsy was found to have an early generalized fibrinous peritonitis. (For further details see pp. 145 and 160.)

Mutual masking of factors. Figs. 15 and 16, A and B, show that the concentrations of both haemoglobin and plasma protein of some of the patients there shown pursued a fluctuating course. The number of factors involved—for instance, further blood loss, later transfusions of blood and plasma, dehydration and various infections—made it often difficult in practice to interpret the cause of these later changes. Moreover the changes seen after transfusion or in association with severe dehydration were often unexpectedly small. Two patients with considerable disturbances of their salt metabolism shown in Fig. 17 have already been discussed: from the changes in their haemoglobin and plasma protein concentrations during the development of the salt shortage it would have been difficult to make a diagnosis of dehydration, and in a number of other cases suffering from similar disturbances still smaller changes were seen.

The probable explanation is that factors tending to cause a rise in haemoglobin or plasma protein concentration were often largely counteracted by others causing a fall. It has already been noted that patients with perforating intestinal wounds show progressive falls in their haemoglobin concentration during the first few days after haemorrhage, and it is probable that such falls masked potential increases in haemoglobin concentration due either to losses of plasma, such as might occur in peritonitis and pneumonia, or to losses of salt solution from the plasma, as would occur in salt deficiency. The picture was further complicated if the patients had also been transfused.

Thus the observed changes in haemoglobin, haematocrit and plasma protein concentrations often gave little indication of salt shortage during the later courses of these patients, even when marked disturbances of salt metabolism were present. This emphasises that estimates of plasma chloride and bicarbonate are essential for the diagnosis of disturbances of salt metabolism.

Conclusions

In the Initial Stages After Injury

1 Untransfused patients with abdominal injuries not perforating the intestines showed changes in initial haemoglobin and plasma protein levels comparable with those shown by patients with limb injuries who had lost similar amounts of blood, that is, they showed haemodilution Therefore the rules already adduced for the measurement of haemorrhage from the haemoglobin and haematocrit concentrations after injury also apply to these cases

2 About half the untransfused patients with abdominal injuries perforating the intestines and estimated to have lost 20 per cent or less of their blood showed haemoglobin levels above 100 per cent (= 16 g per 100 ml) Only two showed levels above 110 per cent It is concluded that such patients may show slight haemoconcentration, but in few is it pronounced (haemoglobin concentration above 112 per cent = 18 g per 100 ml), and its chief cause is thought to be dehydration Very few patients showed evidence of marked plasma protein loss

3 Evidence is insufficient to determine whether, after haemorrhage, the factors tending to cause haemoconcentration ever slowed down the processes causing dilution In some instances they did not

4 Patients with intestinal penetration transfused with plasma showed falls in the level of haemoglobin of the order expected from the estimated blood loss and the quantity of plasma transfused In the great majority of instances plasma transfusions, even of much dilute plasma, caused only small changes in the concentration of plasma protein

5 There is no evidence that patients with intestinal penetration who had lost more than 40 per cent of their blood responded to transfusions of plasma in any way differently from patients with limb injuries who had lost similar amounts of blood and had received similar plasma transfusion This indicates that processes tending to cause haemoconcentration did not interfere with the haemodilution caused by plasma transfusion (see point 3)

In the Later Stages After Injury

6 During the first four to six days after injury a number of patients with abdominal injuries showed further and sometimes considerable losses of red cells that could not be accounted for by blood loss at wounding or at operation No patient showed any gain

7 In addition to the factors that might have acted to cause red cell loss in the patients with limb injuries, two further factors may have been in part responsible in the patients with abdominal injuries These were infections in the lungs and in some cases in the peritoneum, and disturbances of salt and water metabolism

8 The main factors affecting the haemoglobin and plasma protein concentrations seen after operation in those with intestinal penetration and the fluctuations in them were (*a*) the initial haemorrhage, (*b*) the amounts of blood and plasma transfused, (*c*) the associated infections, and (*d*) the state of

hydration of the patient. Because of the number of factors at work it was often difficult to interpret the exact causes of the fluctuations seen. Though in many of these patients other evidence pointed definitely to dehydration through salt shortage, the haemoglobin and plasma protein concentrations observed were usually insufficient of themselves to provide definite evidence of abnormal blood concentration.

9. Very few patients showed evidence of haemoconcentration due to loss of whole plasma. In one haemoconcentration was due to excess blood transfusion.

10. Patients with abdominal wounds, who had lost by initial haemorrhage 10 per cent or less of their blood, had by five to ten days after injury restored their blood volumes to normal, though their total red cell volumes in some cases were reduced to 75 per cent of normal. But patients who had lost 30 per cent or more of their blood, with two exceptions who had received considerable blood transfusion after operation, still had reduced blood volumes at this period. The reduction was in all cases due to lack of red cells, since the plasma volume was normal and in most cases more than normal.

E. Nitrogen Metabolism in Patients with Injuries to the Limbs

Blood urea. A rise of blood urea in the first 48 hr. of injury was common in those who had initially lost more than 40 per cent of their blood, irrespective of the size of the injury, and the greater the blood loss the higher in general was the blood urea. Two factors are known to be responsible: diminished renal function in the period early after injury, and increased formation of urea.

In the patients with large and very large wounds, and initial blood loss estimated at over 50 per cent of the total blood volume, there was very little secretion of urine for the first 8–10 hr. after injury, and the blood urea concentrations reached may be used as a rough method of measuring urea production during this period. At approximately 9 hr. after injury, the blood urea of *Case I*.98 was 70 mg. per 100 ml. and that of *Cases I*.109 and *I*.110 60 mg. per 100 ml.; all these three suffered very large wounds. *Case I*.15, whose wounds were small but whose initial blood loss was estimated at about 60 per cent of his total blood, also had a blood urea raised to 66 mg. per 100 ml. at 9 hr. after injury, but *Case I*.104, who despite very large wounds had a blood loss of only about 30 per cent, had a blood urea of 36 mg. per 100 ml. At this period a raised blood urea seems therefore to depend on blood loss rather than on quantity of damaged tissue.

When the kidneys are not excreting urea, a rise of blood urea of 10 mg. per 100 ml. above normal in a man weighing 70 kg. (11 stones) will be caused by new formation of about 5 g. urea, so *Case I*.98 had formed about 20 g. urea (equivalent to the metabolism of about 60 g. protein) in 9 hr. and *Cases I*.109 and *I*.110 about 15 g.

Case I.91 suffered from large wounds, great blood loss and a prolonged period of low blood pressure which resulted in at least 30 hr. of minimal renal function. Twenty-seven hours after injury his blood urea was 135 mg. per 100 ml., indicating the formation of about 50 g. urea in this period.

Nitrogen balances. In patients with much loss the blood urea usually reaches its peak within 20–40 hr. of injury and thereafter falls as renal function

TABLE 51

*Nitrogen balances in Cases I 109 and I 110**

Patient	Period	Nitrogen intake (g)	Nitrogen output (g)	Balance (g)	Accumulated balance	Blood urea at end of period (mg per 100 ml)
Case I 109	Injury—21hr	88	216	−128	—	80
	1st day (24 hr) after injury	24.5	12.3	+12.2	−115.8	62
	2nd day	12.3	11.0	+1.3	−114.5	45
	3rd day	0.3	16.0	−15.7	−130.2	33
	4th day	1.1	20.5	−19.4	−149.6	37
	5th day	3.5	15.5	−12.0	−161.6	40
	6th day	6.2	17.6	−11.4	−173.0	35
Case I 110	Injury—12½ hr	147.0	217.0	−70	—	106
	1st day (24 hr) after injury	0	22.7	−22.7	−92.7	78
	2nd day	1.0	36.6	−35.6	−128.3	56
	3rd day	1.0	16.5	−15.5	−143.8	44
	4th day	10.3	23.0	−12.7	−156.5	41
	5th day	17.0	27.6	−10.6	−167.1	36
	6th day	1.4	19.0	−17.6	−184.7	30
	7th day	8.3	22.7	−14.4	−199.1	27

* The observations on nitrogen balance were made by Major R. J. Rossiter.

Note. The intake includes all food and transfused fluids, while the output includes nitrogen lost by haemorrhage and in the urine but neglects the nitrogen content of the faeces. The nitrogen losses in the initial period are probably slightly too high since they are calculated by subtracting the nitrogen in the estimated blood volume after injury from the sum of that in the predicted normal blood volume and that in the transfused fluids, this neglects any transfused haemoglobin or plasma protein that passes from the blood stream into the patients' tissues. Both patients were allowed to eat and drink what they liked, and the chief dietary sources of protein were eggs, fish, chicken and bread. The transfused sources were blood, plasma and serum. The urine volumes of *Case I* 109 averaged about 1,400 ml. in 24 hr., varying between 1,000 and 2,000 ml., and those of *Case I* 110 about 2,500 ml. for the first four days, after that rising to 3,500–5,500 ml. a day.

For additional information about the cases mentioned in this section refer to the case index, pp. xi *et seq.*

improves. However, though the blood urea falls, there is an increased production and excretion of urea with a negative nitrogen balance which persists for some days. In Table 51 nitrogen balances made by Major R. J. Rossiter are shown for *Cases I.*109 and *I.*110 to indicate the extent of nitrogen loss in patients suffering very large injuries and very great blood loss. It will be noted that in seven days *Case I.*109 had an accumulated negative nitrogen balance of 173 g. (equivalent to 1080 g. protein) and *Case I.*110 in eight days an accumulated negative nitrogen balance of 199 g. (equivalent to 1250 g. protein). Data on other cases of limb injuries are incomplete, but *Case I.*53, with moderate wounds and initial blood loss estimated as 50–60 per cent of his original blood, while on a light diet excreted quantities of nitrogen of the same order as *Cases I.*109 and *I.*110. All three patients were anaemic, *Case I.*109 having 60 per cent of his estimated normal haemoglobin, *Case I.*110 50 per cent and *Case I.*53 30 per cent at approximately four days after their respective injuries.

F. Urine Pigment

A number of observations were made on the pigment content of the urine. The benzidine method was used as a rough measure of total haemoglobin and myoglobin pigment, and an attempt was made to identify the pigment with the Hartridge reversion spectroscope. The total quantities of haemoglobin pigment in the urines passed soon after injury were generally small, and rarely, except in the large and very large injuries, exceeded 10 mg. per 100 ml. urine. The chief source of the pigment appeared to be red cells. With such low haemoglobin concentrations it was not possible to determine if myoglobin was present.

This may be contrasted with the single case of injury due to prolonged compression ("crush syndrome") seen by us in Italy, in whose first urine passed after injury there was 300 mg. of total haemoglobin pigment per 100 ml. urine and myoglobin and methaemoglobin were readily identified.

It seems, therefore, that in the illness of the cases discussed in this report the excretion of myoglobin played little part. The early urines passed after injury were often deeply pigmented, but the pigments were not identified; they might, however, well repay further study.

G. Salt Metabolism and Calorie Intake of Patients with Injuries to the Abdomen

A number of observations were made on the water, salt and bicarbonate metabolism of patients suffering from abdominal wounds. The observations are far from complete. At first there was a lack of apparatus and reagents, and later, when these were available, the war rapidly drew to a close. They are, however, sufficient to indicate that disturbances of water, salt and bicarbonate metabolism had been responsible for illness and death in a considerable number of patients with abdominal injuries, certainly in a much higher proportion than had been recognized at the time.

DISTURBANCES OF WATER, SALT AND BICARBONATE METABOLISM

According to Black, McCance and Young (1944) marked water shortage unassociated with salt loss causes thirst, dryness of the mouth and throat and difficulty in swallowing The face becomes pinched and there is some loss of power of concentration There is *little change in haemoglobin or plasma protein*, the plasma Na and Cl concentrations rise by up to 10 per cent and the blood urea may be doubled There is some increase in urea production and the osmotic pressure of the tissue fluids rises The urine volume falls to 350–850 ml a day and has a specific gravity of 1030 or greater If the osmotic pressure of the tissues rises too high death ensues

When water intake is adequate, sodium and chloride may be lost from the body in about equal amounts or more chloride than sodium may be lost In the first case, though the volume of the body fluids changes greatly, their *pH* is probably little different from normal In the second case the excess sodium ions combine with dissolved carbon dioxide to form sodium bicarbonate and the resulting increase in the concentration of hydroxyl ions causes *alkalosis*

McCance (1936) has described the effects of marked loss of sodium chloride uncomplicated by alkalosis Subjects who lost up to 30 per cent of their total chloride in 10 days developed mental dullness and a feeling of exhaustion, nausea and anorexia, their cheeks and eyes became sunken and they lost weight Their blood showed haemoglobin and serum protein increases of up to 25 per cent of the normal values, a rise of blood urea to 80 mg per 100 ml and a fall in serum chloride and serum sodium, but bicarbonate concentration was unchanged They showed negative nitrogen balances, one subject losing 33 6 g nitrogen, the equivalent of 210 g protein, over 11 days The kidneys' power of concentrating urea was normal and the subjects could excrete 2 litres of urine a day, but urea clearance tests were low, and early in the course of the experiments sodium and chloride almost disappeared from the urine The giving of sodium chloride caused rapid recovery The underlying disturbance in salt deficiency is *shortage of extracellular fluids (tissue fluid and lymph) from* lack of the Na, Cl and HCO_3 ions required to maintain their osmotic pressure The tissue fluids become hypotonic There is an associated marked reduction in plasma volume

The effects of an increased tissue fluid *pH*, uncomplicated by excess or lack of sodium ions, have not been completely studied It results in a diuresis with excretion of base and bicarbonate, and, if sufficiently increased, tetany

Observations by McCance and Widdowson (1936) suggest that in the presence of marked sodium chloride deficiency an alkalosis has a profound effect on renal function, but in the presence of lesser sodium chloride deficiencies has little effect. Thus, whereas *in a normal subject or one suffering from mild salt deficiency* controlled overbreathing for 30–45 min raised the urine *pH* from 7 0 to 7 7, increased the minute urine volume by 50 per cent, doubled the rate of excretion of sodium, trebled the rate of excretion of potassium and caused a slight fall in the urea clearance, in a markedly salt deficient subject it left the urinary *pH* unaltered (at 5 9), depressed the minute volume to a quarter, depressed the sodium and potassium excretion to about a half and halved the already reduced urea clearance Hence it appears that in severe sodium chloride deficiency the kidney will not excrete base to get rid of the excess bicarbonate, but instead maintains the tissue fluids osmotic pressure, and that the kidney function, already deranged by sodium chloride shortage, is still further deranged by an added alkalosis

A water shortage superimposed on a salt shortage, or on a salt shortage with a bicarbonate excess, presumably results in combinations of the various effects To some extent a salt and a water shortage might mask each other, since the tissue fluids would probably be near isotonic, which might be expected to result in fewer symptoms and smaller variations in serum sodium and chloride concentrations For a recent review on the effects of water and salt shortage the reader is referred to Marriott (1947)

POST-OPERATION TREATMENT

At the conclusion of operation patients were taken to a ward, in many cases latterly a special ward kept for abdominal and large limb wounds. Here, when consciousness returned, they were placed in Fowler's position and continuous suction was applied to a Ryle's tube passed through the nose into their stomachs with the intention of preventing the post-operation abdominal distension seen so commonly in perforating intestinal wounds. Intravenous glucose-saline and, in some cases, transfusions of blood and plasma were given, and courses of sulpha drugs or penicillin or both were instituted. When sulpha drugs were given, 30–200 ml. of a mixture of 4 per cent sodium citrate and 4 per cent sodium bicarconate were often added to the intravenous fluids with the object of preventing sulpha drug crystalluria. Suction was usually continued till the abdomen was soft to palpation and there were signs of peristalsis, which, in the majority of our patients, occurred after 2–4 days. It was continued for longer periods only if abdominal distension or vomiting followed on its cessation. Intravenous fluids were usually stopped at the same time as gastric suction and the patient was put on a light diet, his appetite and thirst controlling the quantity he ate and drank.

Most surgeons adopted a fixed regime during the period of intragastric suction. The patient was usually allowed to drink as much water as he liked. Most of this, with admixed gastric and duodenal juices and swallowed air, was sucked back through the intragastric tube. Patients received 3–7 pint bottles of glucose saline (5 per cent glucose, 0·3 per cent NaCl) and sometimes ½–2 bottles of plasma daily, the amounts of both depending on the views of the surgeon concerned. The volumes of fluid drunk, intravenous fluid given, fluid sucked out from the stomach and urinary output were charted and balanced each 24 hr., although often inaccurately. The patients' fluid balances were generally held to be satisfactory if the fluid charts showed a urinary output of a litre or more and some excess of fluid intake over fluid output.

It will have been noted that the glucose-saline had a weak sodium chloride concentration of 0·3 g. per 100 ml. A common view was that stronger saline solutions were dangerous to patients undergoing prolonged intravenous therapy, and might result in death from pulmonary oedema, of which there was a widespread fear. A quotation from Blackburn and Rob's (1945) article entitled "The Abdominal Wound in the Field" illustrates this statement.

> The quantity of intravenous fluid given after operation is of the utmost importance and the danger of over-administration is particularly great in winter. A standard rate of 5 pints per day (2 plasma and 3 glucose-saline) has been our practice, and it is well to be cautious after the total has reached 15–18 pints Many a patient, in fact, has been over-transfused into his grave by a surgeon in a state of 'ileusphobia', complacent meanwhile in the fluid balance on a chart showing gastric suction and venoclysis figures Better it is to pay heed to the râles at the bases than be bound by figures and fluid charts.

This quotation is referred to again later.

In forward surgical centres there was no equipment to estimate either plasma chloride and bicarbonate or urinary chloride, nor with few exceptions

was it possible to estimate haemoglobin or plasma protein Thus the detection of disturbances in water, salt and bicarbonate metabolism was left to clinical judgment Without experience and biochemical estimations, this was not easy, for instance a number of cases seen earlier on were thought because of the clinical picture to be suffering from alkalosis, but when the plasma bicarbonate was estimated it was found to be within normal limits, and we were led to the erroneous view that the progressive weight loss, mental dulling and death, when they occurred, were due to the associated infections in lungs and peritoneum The great importance of sodium chloride loss without associated alkalosis only became clear with the accurate salt balance observations made by Major Rossiter, some of which are shortly reported

SITES OF LOSS

A man with an abdominal wound is subject to losses of water and salt in many ways Before and after wounding he may sweat, from fear or heat or both As a result of injury he bleeds, and his tissues are damaged and swell Early after injury he may vomit, once or repeatedly, and after operation he loses salt and water via the surgical drains placed in his wounds and via intragastric suction Moreover many patients developed lung infections after operation, most commonly infected lobular or lobar collapses, which have long been known to cause marked disturbance of salt metabolism, while others with intraperitoneal wounds developed localized or generalized peritonitis Finally the patients received, during the period of intravenous feeding and intragastric suction and often for some time afterwards, a low calorie diet which favoured the loss of base combined with ketone acids

REPLACEMENT

During the period of intragastric suction and intravenous feeding the patient was entirely dependent on the intravenous fluids for replacement of his lost salt, and often mainly dependent on them for replacement of lost water

The minimum quantities given daily were three or four bottles of glucose saline solution (5 per cent glucose, 0 3 per cent NaCl) containing 2 7–3 6 g chloride and 1,600–2,200 ml water The maximum quantities were seven bottles of glucose saline and two bottles of serum, containing about 10 g chloride and 5,000 ml water Some surgeons stopped the intragastric suction for certain periods in the day, so that water drunk might not be removed but be absorbed, probably the mildly injured patients did absorb some water at these times, but this is unlikely in the case of those whose injuries had caused considerable disturbance of intestinal function Marriott (1947) has suggested that sodium chloride deficiency may delay water absorption by causing pylorospasm, if this is so, the combination of salt shortage with gut injury will seriously limit water absorption

During the period of intragastric suction the patient was also dependent on the intravenous fluids for his metabolic requirements A few patients were also given liquid feeds, suction being stopped for periods to allow these to be digested and absorbed But a proportion was always sucked back when the

suction was restarted, and it is probably true that the greater the degree of gut disturbance the less was the digestion and absorption. Omitting these patients, the *maximum* daily calorie intake may be calculated from the calorie value of the glucose given in the glucose-saline and the protein content of the blood or plasma transfused; it varied between 300 and 550 a day for, on the average, a period of 2–4 days. Some patients, as we have already said, required intragastric suction and intravenous feeding for 6–10 days because earlier attempts at removal of the suction caused vomiting and abdominal distension, but they too generally averaged the same daily calorie intake; a a very few averaged 700 calories a day.

Two patients illustrating types of disturbance of salt and water metabolism that occurred under such a régime are now described.

*Case B.*51 was wounded on patrol by a machine-gun bullet which entered through the buttock and left through a large hole in the right anterior pubic ramus. In its passage it tore holes in the bladder wall and a loop of ileum, and caused extensive bruising in the scrotum and round the bladder. He probably lost more than 2 litres of blood soon after wounding. At operation, 9 hr. after injury, the torn ileum and peritoneum were repaired, the bladder wound was closed round a Malecot catheter, rubber drains were inserted into the scrotum and into the bladder region, and the external wounds were excised. By the end of operation, which lasted 2 hr, he had received $2\frac{1}{2}$ bottles of plasma, 1 bottle of blood and 1 bottle of serum and his estimated blood volume was 80 per cent of the predicted normal After operation intragastric suction was started, he was given glucose-saline, 0 9 per cent saline, plasma and serum intravenously, and water by mouth, and was treated with penicillin and sulphadiazine. He soon began to lose fluids through the drains in his wounds. By the third day he was showing evidence of marked infection at both lung bases and had probably already developed areas of localized peritonitis.

Fig. 18 summarizes observations made from the third to the eleventh day after injury. The calorie intake, shown in line 11, averaged 400 a day and ranged between 0 and 900 a day. The blood urea (line 2) varied mainly between 50 and 60 mg. per 100 ml. The urine volume (line 9) only fell below 1,500 ml. per 24 hr. on two occasions, so he was not grossly short of water. The total quantity of urea, expressed as urinary nitrogen excreted (line 10), averaged over 20 g. a day, since during this period the patient was lying in bed and receiving little protein, the urea must have been derived from breakdown of his own tissues. Tested on the fifth and eighth days, urea clearance was 65 per cent and 68 per cent normal.

The findings of chief interest concern chloride and bicarbonate metabolism, and are summarized in lines 1 to 8. On the third day the serum chloride and bicarbonate concentrations (lines 4 and 3) were normal, but over the next six days the chloride concentration progressively fell and the bicarbonate concentration progressively rose. Lines 6, 7 and 8 show the grammes of chloride per 24 hr given intravenously or lost in the urine or gastric suction fluid; after the fourth day only traces of chloride were passed in the urine. No estimate can be made of the possibly considerable amounts of chloride lost by sweating (probably not great, since the weather was cool), from the wounds into the dressings and into the effusions passing into infected and damaged tissues. Neglecting them, the chloride given intravenously may be balanced against the chloride lost in the gastric suction and urine, and the balance is indicated by the shaded portion on either side of the line separating chloride given intravenously from that lost by suction. It can be seen that there was only a slight positive chloride balance on the third, fourth, sixth and eighth days and a negative balance on the seventh and ninth days. From the fall in serum chlorides over this period it is clear that the small positive balances were quite insufficient to make up for the other unmeasured sources of chloride loss. By the ninth day the patient was showing signs of gross salt

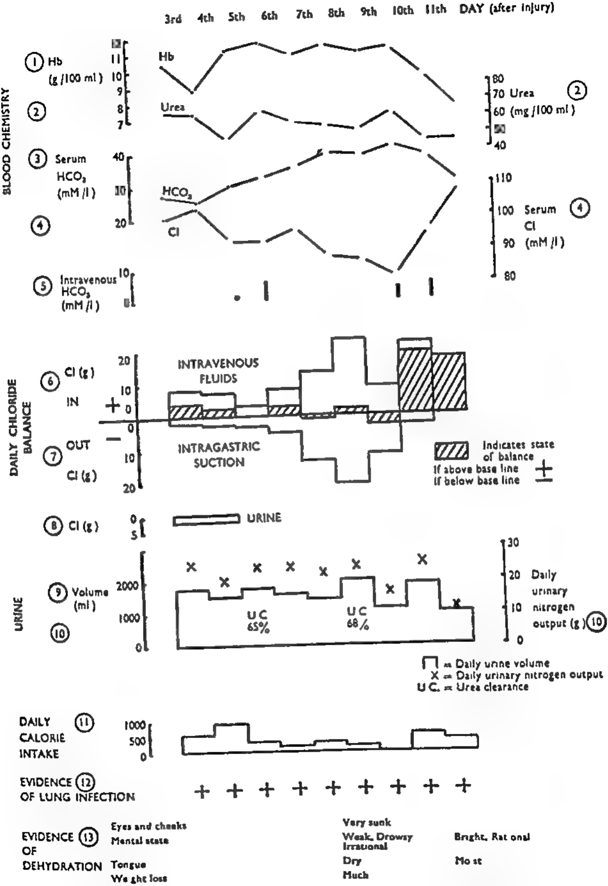


FIG 18 Biochemical and clinical observations on *Case B.51*, showing salt shortage. The chloride balance observations were made by Major R. J Rossiter

deficiency, with sunken eyes and cheeks, great wasting, lassitude and drowsiness. He was irrational and suffered from delusions, and although his blood pressure did not fall he seemed on the point of death.

Large quantities of sodium chloride were given and the improvement was dramatic. He became rational and lost his delusions, drowsiness and signs of dehydration. By the end of the eleventh day it was possible to stop intragastric suction and intravenous feeding, in spite of the continuance of a diarrhoea that had started on the ninth day. On the fifth, eighth, tenth and eleventh days the patient received intravenous alkali.

This patient is typical of a number who became seriously ill, some of whom died. Their primary trouble was salt loss; there was excess loss of chloride over sodium, sufficient to cause some degree of alkalosis. Because they passed adequate amounts of urine of good specific gravity and showed no evidence of latent tetany, they were frequently not recognized as suffering from sodium chloride deficiency. The case quoted received between the third and seventh days 4–9 bottles of glucose saline, or glucose saline and 0·9 per cent saline, each day. The amounts of salt and water given seemed adequate but in fact were not, because of the great quantities of chloride and sodium chloride that were lost by gastric suction. Thus on the eighth day the patient was given 7 bottles of 0·9 per cent saline and 2 of glucose saline, in one of which dried plasma was mixed. Thus 23 g. of chloride were given, but during the same period 21 g. were lost by suction, so that the serum chlorides remained unchanged.

This patient also illustrates the complexity of such post-operation illness. In addition to salt deficiency he was suffering from partial starvation, wound infection, lung collapse and infection, probably from localized peritonitis, and from a marked tissue nitrogen catabolism partly due to injury and partly due to sodium chloride deficiency.

The second case illustrates a different picture, showing the effects not only of salt shortage, but also of water shortage and terminally more marked alkalosis.

Case B.49* was injured by a revolver bullet which entered his abdomen through the left costo-sternal notch, tore two holes across the whole diameter of the jejunum near the duodenum, tore two other smaller holes in the jejunum, tore some small arteries, nicked the left ureter, and passed out through the left loin. He did not lose more than 20 per cent of his blood and was operated on an hour after injury under chloroform anaesthesia, the holes in the intestine being repaired and the vessels ligatured Before, during and immediately after operation he was given one bottle of plasma and three of blood. He was then put on intragastric suction and intravenous feeding, and treated with penicillin and sulphadiazine.

His subsequent course is summarized in Fig. 19 on the same plan as that used for the first patient It will be noted from the figure that the patient had a very low calorie intake (line 11), that he early showed signs of a persisting lung infection (line 12), and that by the third day he was showing the clinical signs of water shortage (line 13), and by the fifth day signs of salt shortage (lines 4 and 8) Smaller quantities of intravenous fluids than usual were given; on the second, third and fourth days he received an average of 2,800 ml of fluid intravenously. His urine volume reached 1,500 ml. only on the third and fourth days and thereafter rapidly declined.

Serum chlorides (line 4), at first normal, fell rapidly to very low levels and at the same time serum bicarbonate (line 3) rapidly rose. Negligible quantities of chloride were lost in the urine after the second day (line 8). During the second, third and

*Further information about *B*49. will be found on pages 138 and 171.

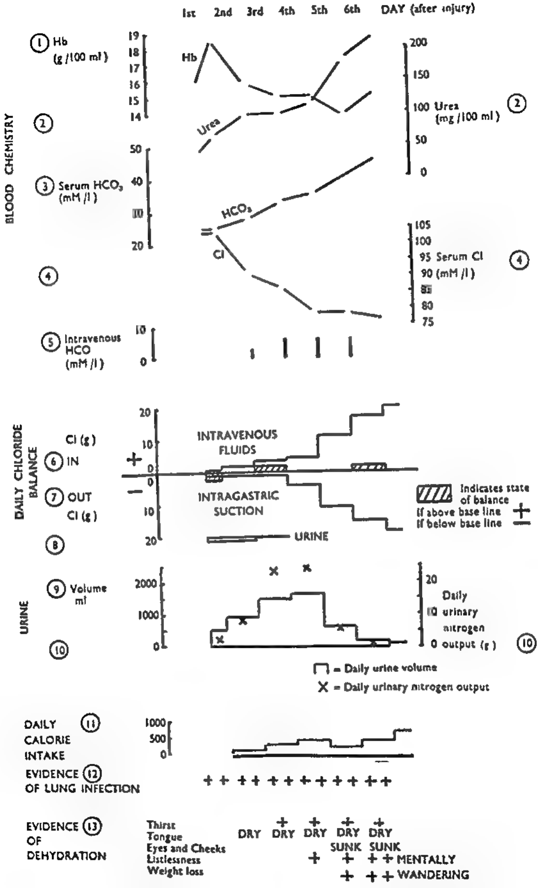


FIG 19 Biochemical and clinical observations on *Case B* 49, showing salt and water shortage and alkalosis

The chloride balance observations were made by Major R. J. Rossiter

fourth days the patient received only small amounts of chloride intravenously (line 6), just sufficient to balance those lost in his gastric suction (line 7) and urine (line 8), and quite insufficient to balance the (unmeasured) loss from other sources which must have been responsible for the great fall in the serum chlorides. Further, though on the fifth and sixth days greater quantities of chloride were given intravenously, at the same time greater amounts of chloride were being lost by gastric suction, so even these were barely balanced on the sixth day. The rise in serum bicarbonate was partly due to loss of hydrochloric acid but was also influenced by administered alkali (line 5), for on the third day 100 ml. and on the fourth, fifth and sixth days 200 ml. of a mixture containing 4 g per 100 ml sodium bicarbonate and 4 g. per 100 ml. sodium citrate were given with the object of preventing sulphadiazine crystalluria. The calculated effects of these amounts on the serum bicarbonate content are shown in line 5. It is assumed that the citrate is oxidized to bicarbonate and the total bicarbonate distributed through 20 litres of fluid, the bicarbonate ion may well be distributed through smaller volumes, in which case these concentrations are underestimates. It will be noted that there was a rapid rise in the blood urea (line 2) in the first two days, associated with a low volume of urine (line 9) and low urinary urea output (line 10), that it remained nearly stationary on the next two days, when nearly 25 g. of urea nitrogen were excreted each day, and that on the fifth and sixth days it again rose as the urine volume declined. On the seventh day the patient showed the symptoms and signs of gross salt deficiency, with pulse rate of 130 and blood pressure of 80/60, and passed very little urine. The blood pressure declined further and was not raised by rapid plasma transfusion, and the patient died. Necropsy revealed (*a*) considerable areas of lung collapse and bronchopneumonia, (*b*) obstruction of the small intestine, (*c*) a moderate degree of peritonitis, and (*d*) a cerebellar pressure cone.

This patient's illness, like that of *B*.51, was complex, consisting of bronchopneumonia, intestinal obstruction, salt and water shortage, and renal failure. The evidence set out makes it probable that a major part of the illness was due to salt and water shortage and associated alkalosis. The evidence that an alkalosis associated with a marked salt loss may cause a profound disturbance of renal function has already been discussed.* On the sixth day the patient received 5 litres of fluid intravenously, but he secreted little urine and showed a further marked rise in blood urea. This indicates derangement of renal function. It is probable that administering sodium bicarbonate, or salts that may be oxidized to form sodium bicarbonate, is a dangerous procedure in the presence of marked salt shortage, since the sodium ion will not be excreted and the alkalosis will persist. This patient, like *B*.51, lost great quantities of chloride by gastric suction.

FREQUENCY OF OCCURRENCE OF WATER SHORTAGE, SALT LOSS AND ALKALI EXCESS

An attempt is made to assess the frequency of disturbances in salt and water metabolism, first in those cases that died and second in those that lived. In many cases this assessment depends chiefly on the records of the clinical pictures and the fluids transfused and lost by suction and in urine. From the close study of the proven cases of disturbances of salt and water

* From time to time soldiers suffering from abdominal injuries were reported to have died from a renal failure not associated with blood transfusion, nor with great blood loss, nor with crushing injury, nor with direct injury to the kidney Since the giving of alkali to avoid sulpha drug crystalluria was common and salt shortage was not uncommon, it seems possible that a number of such renal failures were due to a combination of alkalosis and salt shortage.

metabolism the symptoms and signs became familiar, and we have used the following, symptoms —exhaustion, mental dullness or change, thirst, headache, signs —sunken eyes, lax skin, other evidence of dehydration, marked weight loss, tetany We have also used the volume removed by intragastric suction and the period for which suction was continued, the volume of urine, the amount of fluids lost by diarrhoea, colostomy, etc They have been supplemented by estimations of blood concentration, blood urea, urine concentration and urine urea In a number of cases estimations of blood chloride and plasma bicarbonate were also made, and in a few cases more complete observations of the kind shown in the figures (pp 301 and 303)

Fatal Cases

It is highly probable or certain that disturbance of salt and water balance played a major part in the illness and death of patients *B* 24, *B* 49, *B* 50, *B* 38, *B* 68, *B* 64, *B* 79 and *B* 52, in one other patient, *B* 47, salt shortage and alkalosis may have played a part Excluding this last patient and those dying within 48 hr of injury, in 8 out of a total of 23 deaths salt and water shortage played a prominent part, 6 deaths might have been prevented by making good the shortage A few examples are briefly described

B 38 had three complete divisions and three tears in the small intestine He lived for three days after operation, the weather was very hot He averaged a total of 4,000 ml fluid intravenously a day, but was given intravenous alkali and lost large amounts of fluid by gastric suction Over his last 24 hr his plasma bicarbonate rose to 58 mM/litre and he developed tetany He developed renal failure, probably chiefly caused by salt shortage and alkalosis, and terminally his blood urea was 400 mg per 100 ml

B 24 had a hole in the right buttock leading into the rectum After operation he was treated by gastric suction and intravenous fluids until the tenth day, when the treatment was stopped After three days it was begun again, and continued until his death two days later The weather was very hot and the patient sweated much Considerable amounts were removed by gastric suction and only 5 g of sodium chloride at most were given intravenously each day He lost much weight and became listless and flabby and finally drowsy, he was very thirsty and his eyes became sunken Blood urea rose in the first three days to 150 mg per 100 ml, then fell to remain between 60 and 80 At necropsy the body was very wasted and the tissues were dry There was a large abscess in the region of the rectum, and bilateral bronchopneumonia Water and salt loss were thought to have played a large part in his illness Inadequate fluids and salt had been given for fear of pulmonary oedema

B 50 had holes *in the bladder, jejunum and ileum* and lived for seven days after operation in very hot weather He was given intravenous fluids with intragastric suction for six out of the seven days, an average of 7 5 g of NaCl being given each day He lost considerable amounts of gastric suction fluid and sweated much, on several occasions he also vomited large quantities He developed thirst, dryness of the throat, sunken eyes and face and evidence of marked dehydration, gross weight loss and personality changes His blood urea remained between 100 and 160 mg per 100 ml Shortly before death the plasma bicarbonate was 25 mM/litre At necropsy the body was found to be very wasted, with some localized peritonitis and areas of pneumonia and collapse in both lungs

B 79 had multiple holes in jejunum and ileum, stomach and gall bladder At operation some of these holes were not detected, and gall bladder and jejunal fistulae soon

developed. He lost great quantities of fluid from the fistulae as well as by gastric suction and sweating. The weather was very hot. He lived 43 hr. after operation, and developed a blood pressure of 70/50, pulse rate of 120–140, marked vasoconstriction, thirst and a dry mouth, with a very small urine output and a blood urea rising to 200 mg. per 100 ml. In these 43 hr. he received a total of 18 g. NaCl, quite inadequate to replace his losses. The primary cause of death was gross loss of intestinal fluids; at necropsy only an early peritonitis and unclosed wounds were found to account for death.

Surviving Cases

Among those patients surviving, five showed evidence of considerable salt shortage, with or without water shortage (*B*.56, *B*.39, *B*.71, *B*.51, *B*.77), and at least five other cases showed lesser degrees. One case that died from another cause also showed evidence of marked salt shortage for a period (*B*.30). Examples are briefly described.

[*B*.51 has already been described on p. 300.]

B.39 (p. 143) suffered from a few perforations in the small intestine and from minor wounds. The perforations were closed and after operation he was put on intermittent gastric suction but no intravenous fluids. In the next three days he became tired and mentally dull, lost his appetite and developed a dry mouth and lung infection. On the third day after operation the plasma chlorides had fallen to 72 mM/litre and the plasma bicarbonate was 30 mM/litre. After salt infusion the patient showed great improvement, with a rise in plasma chlorides, a fall in blood urea from 76 to 40 mg. per 100 ml. and a fall in haemoglobin from 11 to 9 5 g. per 100 ml.

B.56 (p. 135) pursued a long and complicated course. After wounding he lay out in a very hot sun for 4 hr., and 8 hr. later had a temperature of 105° F. (40 6° C.) His main wounds were holes in the ascending colon, which was exteriorized. After operation the weather was very hot. He lost large amounts of fluid by gastric suction and vomiting, and was given much intravenous alkali. He became mentally dull and drowsy, at times almost unconscious, and wandered mentally at night; he lost much weight. Over five days, although he was passing about 1,000 ml. urine a day, his blood urea rose to 260 mg. per 100 ml. and his urea clearance was estimated to be only 12 per cent of normal. On cessation of gastric suction and intravenous feeding he gradually showed improvement By two weeks after wounding his blood urea had fallen to 130 and his urea clearance had risen to 45 per cent of normal. He was mentally clear and had a good appetite. Three weeks after wounding his blood urea was 48 mg. per 100 ml. and his urea clearance was 80 per cent normal. This patient was treated in exactly the same way and at the same time as *B*.38, who died from alkalosis. He is thought to have suffered from salt shortage and alkalosis. His renal condition cannot be explained as due to local injury, blood loss or transfusion

Because of the importance of establishing the prevalence of disturbance in salt and water metabolism in such cases, brief details of five further cases of abdominal injury treated with gastric suction are now given. These cases were observed and treated by Major Chute, Captain Cleghorn and other members of the No. 1 Canadian Medical Research Laboratory, R.C.A.M.C. I have been able to collect these details through the kindness of Dr. Grant Lathe, who placed the records at my disposal and was responsible for the biochemical investigations.

Case 150 Injuries:—tear in liver, perforation of stomach, torn femoral artery, other flesh wounds and compound fractured ulna. Much blood was lost. Before and during operation he was transfused 2,000 ml. blood, 1,000 ml. glucose saline and 800 ml.

plasma, the femoral artery was ligated After operation he was treated for three days with indwelling gastric suction and daily quantities of intravenous fluids, 2,500–3,500 ml glucose saline and 400–800 ml plasma containing 25–50 g protein On the fourth and fifth days after operation his plasma chloride was 85 millimols, his blood urea was 190 mg per 100 ml and there was little chloride in the urine Subsequently his leg required amputation because of gangrene and later he died after developing a gastric fistula

Case 159 Injuries —torn liver, through and-through wound of ileum He was transfused before, during and immediately after operation with 800 ml blood, 1,200 ml plasma and 1,500 ml glucose saline He lived for five days after operation He was treated by gastric suction and intravenous infusions, receiving 1,500–4,000 ml glucose saline and at least 400 ml blood or 300–500 ml plasma a day He passed 1,080 ml urine on the first day after operation, 125 ml on the third, 70 ml on the fifth On the third his plasma chloride was 85 millimols, his blood urea 315 mg per 100 ml, on the fourth day plasma chloride was 80 millimols, blood urea 282 mg per 100 ml He died on the fifth day after operation, and necropsy showed peritonitis, collapse of the lower lobes of both lungs and both kidneys large and pale

Case 170 Injuries —six holes in jejunum, through-and-through wound of the descending colon, compound fracture of the ilium, gross soft tissue wounds He was transfused before, during and after operation 1,200 ml blood, 2,100 ml plasma and 1,500 ml glucose saline For the first four days after operation he was treated with gastric suction and passed 1,200–4,000 ml urine a day He was given daily 1,500–2,500 ml 5 per cent glucose solution, 1,000 ml plasma and volumes of glucose saline varying from 0 to 2,500 ml Plasma chlorides fell to 76–82 millimols and blood urea rose to 165 mg per 100 ml Plasma chlorides remained low after cessation of the gastric suction and it was noted that by the second week of his illness he had lost a lot of weight He eventually recovered

Case 174 Injuries —tear in hepatic flexure of colon, torn right kidney, retroperitoneal haematoma At operation nephrectomy was carried out He was transfused before and during operation with 800 ml blood and 3,200 ml plasma After operation he was treated with intragastric suction and infusions of 5 per cent glucose solution, plasma, blood and rather small amounts of glucose saline He averaged 500 ml plasma, on some days more, and 1,500–2,500 ml glucose a day, supplemented on some days with various amounts of glucose saline solution On three days he was given 400 ml of blood By the second day plasma chlorides had fallen to 85 millimols, blood urea had risen to 278 mg per 100 ml and daily urine output had fallen to 100 ml During the next seven days the urinary chlorides fell to 77 millimols, the blood urea rose to 540 mg per 100 ml and the urinary volume rose to a maximum of 1,100 ml in 24 hr He became lethargic and then semicomatose At necropsy there was no peritonitis, but there was a large spleen, a pale liver and a collapsed lower lobe of the right lung The remaining kidney looked normal

Case 179 Injuries —transection and bruises of jejunum, holes through descending colon and bruises of transverse colon, compound fractures of left femur, right foot and right wrist Before and during operation he was given 1,600 ml plasma and 1,200 ml blood, and after operation 400 ml blood and 1,000 ml plasma. He was treated for five days after operation with indwelling gastric suction and intravenous infusions of glucose saline, plasma and blood, he averaged 1,500–3,000 ml glucose saline and 500–1,000 ml plasma a day On occasion 5 per cent glucose solution was given in place of the glucose saline During the first five post-operative days 1,600 ml of blood were transfused Daily urine volumes varied from 700 to 2,200 ml, plasma chlorides fell progressively to 83 millimols and blood urea rose to 78 mg per 100 ml When intragastric suction ceased he ate well and made a good recovery

It should be noted that in these brief case histories the quantities of blood shown refer to undiluted whole blood and the quantities of plasma to plasma with an approximate protein content of 6 g. per 100 ml. The volumes of diluent given with blood and plasma, which on occasion were considerable, are not shown. The glucose saline contained 0 3 per cent sodium chloride and 5 per cent glucose.

Though neither estimates of plasma bicarbonate and of the daily quantities removed by gastric suction nor chloride balance observations are available, since at the time other problems were being studied, the evidence strongly suggests disturbances of salt and water metabolism. It is suggested that *Case* 159 died from salt deficiency and alkalosis (compare our *Case B*.49) and *Case* 174 from salt deficiency superimposed on reduced renal function following nephrectomy. These cases received considerable quantities of intravenous fluids, but not sufficient to replace salt loss if large volumes were being removed by gastric suction. *Cases* 170, 174 and 179 received 5 per cent glucose in place of glucose saline, so that their sodium chloride intake was even further restricted. These cases provide evidence that disturbances of salt and water metabolism occurred and were not uncommon in other commands besides our own.

COMMENT

The observations noted here establish the importance of disturbances of salt, bicarbonate and water metabolism in abdominal cases. We have already pointed out the complexity of the illness from which these patients suffered: infections of lungs and peritoneum, semi-starvation and a gross tissue catabolism. The question arises, what deleterious effects did the disturbances of salt and water metabolism have? A gross degree of salt deficiency may cause a fall in blood pressure and death from circulatory failure, but falls in blood pressure were only rarely seen, e.g. in *B*.79 and *B*.49. An alkalosis combined with a salt deficiency, or perhaps either separately if sufficient in degree, may cause renal failure, as for instance in *B*.49 and *B*.38. Gross salt deficiency may increase tissue catabolism. Clinical experience suggests that shortage of salt and water makes the body less resistant to infection, and that the combination of infection and salt deficiency is far more often fatal than either separately; Addison's disease well illustrates this point. The disturbance of salt metabolism in pneumonia is well known, and it is claimed that if enough sodium chloride is given to prevent dehydration a beneficial effect is exerted on the course of the disease (Peters and Van Slyke, 1931). We have already noted the fear of intravenous fluids because of the presumed risk of pulmonary oedema, a fear well illustrated by the quotation from Blackburn and Rob (1945) given on p. 298. When evidence of lung infection was detected the fear was increased, so that it may well be that in a number of cases the lung infection was aggravated by the withholding of saline, and that "pulmonary oedema" was due not to an excess of intravenous fluids, as commonly thought, but to a lack of them.

There was almost certainly a much greater disturbance of mineral metabolism than our observations have indicated, for these have done no more than

touch the surface of these deranged mechanisms* The important practical point is that in many cases the body appears able to right such disturbances of itself if sufficient quantities of sodium chloride are given

CONCLUSIONS

Our results suggest that perhaps 20 per cent of those dying from abdominal wounds might have been saved and that the clinical courses of many of those recovering might have been easier if adequate salt and fluid had been given Five factors militated against adequate treatment

(1) The results of disturbances of salt and water metabolism were often not clearly recognized and therefore went uncorrected

(2) The glucose saline provided had too low a chloride content for the patient who required a prolonged period of intragastric suction or who lost any considerable quantity of gastric and intestinal juice*

(3) Even the simplest means for determining the chloride content of urine and gastric suction fluid, or the chloride and bicarbonate content of plasma, were lacking

(4) There was an exaggerated fear of pulmonary oedema

(5) The practice of giving alkali to salt-deficient patients was not recognized to be dangerous

* *Note added in proof* Since this was written the importance of disturbances in potassium levels in states of dehydration has become apparent For a recent review see Darrow, D C, *New Eng J Med*, 1950, pp 978 and 1014

SUMMARY

(1) The clinical features of the complex illness arising from limb and abdominal injuries are fully described, and illustrated by the histories of numerous patients, who have been followed through the whole course of illness, before, during and after operation.

(2) Clinical observations are combined with haematological and other investigations, including estimates of blood volume (T1824 method) and haemorrhage. The value of the estimates is assessed, and they are concluded to be of the right order.

(3) The clinical features, and in particular the circulatory disturbances are found to combine in various patterns that change during the course of illness.

(4) The factors responsible for these patterns include the site and extent of the injury, the haemorrhage, the nervous and emotional stimuli, the temperature of the surrounding air, the age of the patient, and the treatment administered before, during and after operation.

(5) Of these factors haemorrhage is by far the most important, so that early and adequate blood transfusion is the most important remedy.

(6) Patients who continue to be ill in the late post-operation stage suffer from metabolic, erythrocytic or renal disturbances (often the results of inadequately treated haemorrhage), infection, or fat embolism. Those with abdominal injuries are liable to suffer disturbances of the salt and water metabolism caused by intragastric suction.

(7) The prevailing conceptions of "shock" do not provide a satisfactory basis for elucidating the causes of the various patterns of illness or for guiding treatment. In particular, they are inadequate for assessing the amount of haemorrhage, the reduction of blood volume, and the amount of transfusion required to restore blood volume to a safe level.

(8) In the initial stages of illness these assessments can almost invariably be made with sufficient accuracy by the use of certain clinical features. An estimate of the volume of tissue damaged provides a valuable index of blood loss in limb injuries, although not in abdominal injuries, while in both limb and abdominal injuries, provided the patient has not been transfused and infection has not developed, the systolic blood pressure is an equally valuable index of the level of blood volume. Further information of diagnostic value can be derived from the various patterns mentioned above.

(9) Special attention is paid to patients with limb injuries defined as "very large," and their high mortality rate is attributed to failure to recognise the grossness of the haemorrhage and to give sufficient blood by vein sufficiently early and quickly. In such cases the haemorrhage is of the order of 50 per cent or more of the total blood; they urgently require very large transfusions and respond well to them.

ACKNOWLEDGEMENTS

ALTHOUGH this Report appears under our two names, we wish to make clear that it is the outcome of observations by all the members of the Clinical Research Unit and No 1 Traumatic Shock Team Major R P Harbord was in large part responsible for the clinical observations relating to anaesthesia

We are much indebted for the help given us by those in charge of the various hospitals at home and abroad in which we worked, and by our more immediate colleagues at these hospitals, who not only allowed us access to their cases but often assisted in the observations

The work in Italy was greatly facilitated by our administrators, and particularly by Major-Generals L J Poole and W C Hartgill, and by Brigadiers Stanley Arnott, Gordon Cheyne and F A R Stammers We owe much to their help in overcoming the difficulties inseparable from work on the battlefield

We gratefully acknowledge the support given to the work throughout by the Medical Research Council

About half the Home patients and almost all the cases in Italy were observed by members of the team, for the remainder we are indebted to the observations of others *

* We gratefully acknowledge the case records received from the following observers and made use of in this report *Home Series* Dr R F Ball, Dr R D Blachford, Dr Helen Brown, Dr James Dow Professor O G Edholm Major Ellis R A M C Dr C J Gavey, Dr J C Ledingham Dr John Lipscomb, Professor J McMichael, Dr G A R Miles, Dr P L Mollison, Dr T Parkin, Professor G W Pickering, Squadron Leader W W Reid R A F V R Captain Rocke Robertson C A M C, Dr F Robertson, Dr J R Tasker, Dr Van der Walt, Brigadier L E H Whitby Mr A W Wilkinson, Professor W C Wilson *Italian Series* Captain R F Maybin R A M C, Captain T B McMurray, R A M C, Major C G Rob, R A M C

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